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**EFFECT OF COUNSELLING AND CONDOM PROVISION ON
SEXUAL BEHAVIOUR OF HETEROSEXUAL HIV DISCORDANT
COUPLES AS PART OF AN HIV PREVENTION TRIAL
SOUTH AFRICA**

Dr Phiona Enid Namale

NMLPHI002

Master of Public Health (Epidemiology)

University of Cape Town

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Supervisors:

Dr David Coetzee

Department of Infectious Diseases

School of Public Health & Family Medicine

University of Cape Town

A/Prof Francesca Little

Department of Statistical Sciences

University of Cape Town

DECLARATION

I, Phiona Enid Namale hereby declare that the work on which this dissertation is based is my own except for where it has been acknowledged and referenced. None of this work has been or is being submitted for another degree in another University

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Thesis Abstract

South Africa as a country has a high HIV prevalence. Due to the fact that HIV transmission is predominantly heterosexual, HIV discordant couples are a high risk group for HIV. A number of HIV prevention interventions have been targeted at HIV discordant couples including HIV testing and counselling. An HIV prevention trial assessing the efficacy of daily acyclovir on HIV transmission among heterosexual HIV discordant couples was undertaken in South Africa. We conducted a before and after study with the aim of evaluating the effect of HIV counselling and condom provision on sexual behaviour of the heterosexual HIV discordant couples enrolled in this prevention trial. Counselling was offered monthly to 196 HIV-positive index participants and quarterly to their HIV-negative partners. Couple counselling was offered to couples quarterly and free condoms provided at every visit. Self reported frequency of protected sexual acts in the preceding month was collected using interviewer assisted questionnaires at each counselling visit for one year. Urine pregnancy tests confirmed pregnancies while clinical examination and laboratory tests were used to diagnose genital tract infections. At the end of one year, the incidence rate ratio of protected sexual acts among couples was 50% higher than at baseline. Presence of non-primary partners among index participants and earning by partner participants reduced the incidence rate ratio of protected sex by 25% and 6% respectively. Six percent of the female index participants got pregnant during the one year of follow up, with an incident rate of 2.02 per 10000/year. The prevalence of genital tract infections decreased with time during the study.

These findings suggest that counselling and provision of condoms to heterosexual HIV discordant couples significantly increased the rate of condom use thus reducing the risk of STIs and HIV transmission.

Dedication

I would like dedicate this dissertation to the memory of my brother Micheal Kawuma Mukasa who left us before we were ready to say good bye.

University of Cape Town

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Abbreviations

ABC	Abstinence Be faithful Condom use
AIC	Aikaikes Information Criterion
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
CD4	Cluster of Differentiation 4
CI	Confidence Interval
DALYS	Disability Adjusted Life Years
DHS	Demographic Health Survey
DNA	Deoxyribonucleic Acid
EC	Ethics Committee
EIA	Enzyme Immunoassay
GUD	Genital Ulcer Disease
HCT	HIV Counselling and Testing
HIV	Human Immunodeficiency Virus
HSRC	Human Sciences Research Council
HSV	Herpes Simplex Virus
IQR	Inter-Quartile Range
IRB	International Review Board
LGV	Lymphogranuloma Venereum
LNMP	Last Normal Menstrual Period
OR	Odds Ratio
RCT	Randomised Control Trials
SE	Standard Error
STI	Sexually Transmitted Infection
USD	United States Dollar
VCT	Voluntary Counselling and Testing

PART A: PROTOCOL

EFFECT OF COUNSELLING AND CONDOM PROVISION ON SEXUAL BEHAVIOUR OF HETEROSEXUAL HIV DISCORDANT COUPLES AS PART OF AN HIV PREVENTION TRIAL SOUTH AFRICA

1.0 INTRODUCTION

Sub-Saharan Africa accounted for 67% of the 33 million people globally living with HIV/AIDS in 2007 and Southern Africa as a region contributed 35% of this total ⁽¹⁾. The HIV epidemic in South Africa is described as hyper-endemic given that more than 15% of the adult population (15 to 59 years) are living with HIV ⁽¹⁾. The HIV prevalence in 2008 in the Western Cape Province of South Africa was 5.3% in the 15 to 49 year age group ⁽²⁾.

Heterosexual transmission between regular couples is an important mode of HIV spread in Sub-Saharan Africa ^(1,3). HIV discordant couple refers to the situation in which only one member of a sexual partnership is HIV infected ⁽⁴⁾ and there is evidence of HIV discordance in Africa ⁽⁴⁻¹⁰⁾. High rates of HIV transmission have been found between HIV discordant couples who are often in stable or long term partnerships but unaware of each other's HIV status ^(6,11). These couples may be married or cohabiting. In Sub-Saharan Africa approximately 50% of HIV-infected persons are in an HIV discordant relationship ⁽¹²⁾ and therefore discordance is a major contributor to the spread of HIV. HIV-negative partners within HIV discordant relationships are a particularly high risk group for HIV acquisition. The focus of prevention strategies among these couples could therefore substantially reduce HIV transmission rates.

A number of strategies have been implemented to prevent the spread of HIV including; provision of early diagnosis and treatment of sexually transmitted infections, treatment of

eligible HIV infected persons with anti-retroviral therapy and counselling on HIV risk reduction (abstinence, condom use and monogamy) ^(13,14).

In 2007/2008 a phase III prevention trial was undertaken in 12 sites in Africa to determine if suppression of *Herpes Simplex II* virus using daily acyclovir reduces HIV transmission among heterosexual HIV discordant couples. Free condoms and counselling on HIV prevention were offered to all study participants during the one year follow up period. We sought to evaluate the effect of the counselling and condom provision on the sexual behaviour of the HIV discordant couples enrolled at one of the South African trial sites.

2.0 PROBLEM

Many studies on HIV and its prevention are being conducted in Africa due to the high rate of HIV transmission in the region. There is a need for measures to prevent HIV transmission in such studies using standard practices already known to prevent transmission. For instance, counselling on HIV prevention and the provision of condoms are offered as part of all HIV prevention trials to encourage participants to practice safer sex. However knowledge on the effect of these interventions on sexual behaviour of heterosexual HIV discordant couples is limited. Studies among heterosexual HIV discordant couples are limited in South Africa, more so those enrolled in prevention trials.

3.0 JUSTIFICATION

The existence of unsafe sexual behaviour among HIV discordant couples is well documented ^(7,15). In a study of the sexual behaviour of 963 cohabiting heterosexual HIV discordant couples less than 3% of couples reported condom use prior to HIV counselling and testing (HCT) and enrolment into the study ⁽¹⁶⁾.

All studies using HIV-discordant couples provide counselling and education on ways to prevent the spread of HIV, as well as condoms to participants. It is the responsibility of researchers to ensure that the risks and benefits of research are balanced in every study. Knowledge on the effect of these prevention strategies on sexual behaviour of HIV discordant couples is limited and yet relevant to subsequent approaches in HIV prevention among these couples and the general population ⁽¹⁷⁾.

Mathematical models estimated that if a couples' intervention could reduce HIV transmission among HIV discordant couples by 13% every year, 35% to 60% of heterosexually transmitted infections would be averted ⁽¹⁸⁾. It is therefore important to determine if HIV prevention interventions are effective in reducing transmission risks.

4.0 RESEARCH QUESTION

Do counselling and the provision of condoms to heterosexual HIV discordant couples as part of an HIV prevention trial lead to less risky sexual behaviour?

5.0 OBJECTIVES

5.1 Main objective

- To identify whether counselling and the provision of condoms as part of an HIV prevention trial leads to less risky sexual behaviour of heterosexual HIV discordant couples.

5.2 Subsidiary objectives

- To assess condom use amongst heterosexual HIV-discordant couples.
- To describe the incidence of pregnancy among heterosexual HIV discordant couples.

- To measure the prevalence of genital tract infections among the heterosexual HIV discordant couples.

6.0 LITERATURE REVIEW

6.1 HIV Discordance in Africa

HIV discordance refers to a situation in which only one member of a sexual partnership is HIV infected ⁽⁴⁾. There were regional differences in prevalence of HIV discordance in a prevention trial assessing the impact of HSV-2 suppression with acyclovir compared to placebo in reducing HIV-1 transmission among HIV discordant couples ⁽⁹⁾. Among all couples tested in the 12 study sites in Eastern and Southern Africa, HIV discordance ranged from 36% to 85% with an overall rate of 49%. In South Africa the prevalence of HIV discordance was 27% in 2008 ⁽⁹⁾. Studies among HIV discordant couples enrolled in prevention trials in South Africa are limited. Condom use is an important means of HIV prevention among sexually active heterosexual HIV discordant couples ⁽¹⁹⁾.

6.2 Effectiveness of condom use

Condom promotion strategies have been widely implemented in Africa to reduce the transmission of HIV. A longitudinal study of 343 HIV-negative steady partners of HIV infected men indicated that the use of condoms during every sexual encounter was associated with a 90% reduction in risk of HIV transmission ⁽²⁰⁾. In a European multi-country prospective study among HIV discordant couples to determine transmission of HIV to negative partners, half of the couples reported using condoms at every intercourse and no HIV transmission occurred among these couples ⁽²¹⁾. In a Haitian HIV discordant couples study, among the 177 couples (37%) who remained sexually active after enrolment, the HIV seroconversion rate was 5.4 per 100 person year. The infection rate was 1.0 per 100 person years among those who reported that they always used condoms (2.4% of 42 couples),

compared with 6.8 per 100 person years among those who used condoms inconsistently or not at all ⁽²²⁾.

Furthermore, a Cochrane review to estimate condom effectiveness in reducing heterosexual transmission of HIV concluded that consistent use of male condoms resulted in an 80% reduction in HIV incidence ⁽²³⁾. Consistency was defined as using a condom for every act of penetrative vaginal intercourse.

6.3 Effects of HIV testing and counselling on sexual behaviour

Studies have shown that there was an increase in self reported use of condoms by heterosexual HIV discordant couples following confidential HIV testing and counselling ^(16,24-27). In a prospective study of 60 HIV discordant couples in Kigali, Rwanda, the proportion of discordant couples using condoms after HIV testing and counselling increased from 4% to 57% after one year of follow up, $p < 0.05$ ⁽²⁴⁾.

Following voluntary counselling and testing (VCT), at a VCT centre in Lusaka, Zambia, more than 80% of reported sexual acts among 963 cohabiting heterosexual discordant couples included condoms compared to 3% prior to the intervention, $p < 0.05$ ⁽¹⁶⁾.

As part of a longitudinal study, husbands and cohabiting partners of 648 Rwandan women were recruited in a male-focused HIV counselling programme in Rwanda, Kigali. All women and 37% of the men had previously received VCT services. There was increase in self-reported condom use after one year of follow-up in all couples. A condom ratio (number of acts of penetrative sex with condoms as a proportion of the total number of sex acts) was used. Regular condom users were couples in whom both partners independently reported condom use resulting in a condom ratio that exceeded 0.9. At the end of one year, the

proportion of couples who qualified as regular condom users increased from 5% to 65% among the HIV discordant couples, $p < 0.05$ ⁽²⁶⁾.

A systematic review that included a meta-analysis on effects of HIV testing and counselling on sexual behaviour was done on studies conducted between 1985 and 1997 ⁽²⁷⁾. This review concluded that after HIV testing and counselling, HIV-positive participants and HIV discordant couples increased condom use more than HIV-negative and untested participants. The weighted mean effect size among the serodiscordant couples was $d = 1.31$ (95% CI = 1.14 – 1.48, Q statistic = 147.43, $p < 0.001$) and studies were homogenous. In this study the standardised mean difference index (d) was used and positive effect sizes indicated reductions in risky sexual behaviour ⁽²⁷⁾. An effect size of ± 0.2 was considered small, and above ± 0.8 was large ⁽²⁸⁾.

Another systematic review and meta-analysis on effectiveness of behavioural interventions in developing countries included studies conducted between 1990 and 2006. Three of the studies measured condom use following HIV counselling and testing among HIV discordant couples. Pooled data from these studies ($n = 312$) showed condom use increased (OR: 67.38; 95% CI: 36.17–125.52). The Q statistic of 0.96 showed no statistically significant heterogeneity $p = 0.62$; $I^2 = 0.000$) across these three studies. ⁽²⁵⁾.

Only one prevention trial on the effectiveness of HIV testing and counselling was identified in Africa. Voluntary counselling and testing was associated with a reduction in incidence of sexually transmitted infections in this randomised control trial in Kenya ⁽²⁹⁾. Respondents who reported unprotected sexual intercourse with non-primary partners were twice as likely to have an incident STI compared to those not reporting unprotected sex with non-primary partners ($p = 0.01$). Those who reported unprotected sex at baseline were twice as likely as

those who did not report this to have an incident STI, $p < 0.025$, after adjusting for unprotected sex with non-primary partner at 6 months.

Studies on the effectiveness of HIV testing and counselling as part of HIV prevention trials were limited.

7.0 METHODOLOGY

7.1 Study Design

This will be a before and after study analysing secondary data from an HIV prevention trial.

Study design of the primary study

The trial was a randomised, double blind prevention trial. Half of the HIV-positive index participants were given acyclovir to suppress genital Herpes and half were given a placebo. Information on sexual behaviour was collected prospectively from the cohort of 'index participants' (HIV-positive) and their partners referred to as 'partner participants' (HIV-negative). This prevention trial was conducted in seven countries, one of which was South Africa. There were three sites in South Africa but only data from the Cape Town site will be used. Couple counselling and education were offered to all participants during the follow up period and condoms provided. Individual counselling was offered if preferred by participants. Participants were followed for 12 months in this study.

7.2 Population and Sampling

The study was conducted in the Klipfontein sub-district, Cape Town, Western Cape province of South Africa. Heterosexual HIV-discordant couples in which the HIV-infected partner had a CD4 cell count of at least 250 cells/mm³ at screening were enrolled.

Heterosexual couples were defined as sexual partners of the opposite sex who were married, living together, or who otherwise considered the other a primary partner. In order to be considered eligible for this study, both partners had to expect to maintain their relationship for at least 24 months. The index participant could be either a man or a woman.

The index participant could have had more than one partner who could also have participated in the study (e.g. an HIV-infected man with multiple wives or a wife and steady girlfriend). The partner participant was allowed to enrol in the study with only one primary partner. However, they were not excluded from participating in the study if they had more than one sexual partner.

7.3 Data collection

Information on sexual behaviour was collected using interviewer-assisted questionnaires. The index participants were interviewed on a monthly basis while their partners were interviewed quarterly. Couples were asked to report frequency of sexual acts and frequency of those sexual acts in which condoms were used. Participants were asked to report on sexual behaviour in the preceding month to reduce recall bias. HIV counselling was offered at each visit and couples were counselled together quarterly when both partners were scheduled for a visit. Both partners underwent not only an HIV risk behaviour interview but also an interview to determine if they had symptoms of an STI. Treatment of STIs was based on clinical findings and/or laboratory confirmation. The HIV-negative partners underwent HIV testing every three months. Condoms were provided at every visit. Pregnancy tests were performed on female index participants quarterly and when pregnancy was suspected.

7.4 Recruitment strategies

Recruitment strategies included partnering with existing VCT centres and outreach workers, public promotion of couples VCT by well known members from the respective societies and

community organizations such as churches and community mobilization around the importance of couple testing for HIV. Advertisements were placed on bill boards, in newspapers and radio talk sessions on the importance of the determination of the HIV status of couples. Recruitment materials included education on the probability of being HIV discordant; the risk of transmission of HIV and emphasized the benefits of couples VCT with specialized counselling services.

7.5 Inclusion and Exclusion Criteria

7.5.1 Couples' inclusion criteria

- Couples were sexually active (defined as having had vaginal intercourse with the partner participant at least three times in the last three months)
- Couples planned to remain in the relationship for at least 24 months.
- Both index and partner were at least 18 years of age
- Both index and partner were able and willing to provide written informed consent to be screened for and to take part in the study.
- Both index and partner were able and willing to provide adequate locator information in order to minimise loss to follow up.

7.5.2 Index participants' Inclusion criteria

- HIV-infected based on positive Enzyme Immune Assay.
- CD4 cell count of at least 250 cells/mm³.
- No history of any clinical AIDS-defining diagnoses.

7.5.3 Index participants' Exclusion Criteria

- Current use of combination antiretroviral therapy

- Known history of adverse reaction to acyclovir.
- Known history of persistent genital ulcers unresponsive to episodic acyclovir therapy.
- Pregnant, based on participant self-report or urine testing performed by study staff.

7.5.4 Partner Participants' Inclusion Criteria

- HIV-uninfected based on negative HIV EIA tests.

7.6 Sample size calculation

Using a sign test of equality of paired proportions with a 5% two-sided level of significance, a sample size of 120 pairs will have 86% power to detect a difference in proportions of 0.2 (20%) when the proportion of discordant pairs is expected to be 0.50. Allowing for 25% non-response rate, a further 30 pairs would be required giving a sample size of 150 HIV discordant couples.

7.7 Variables

The main variables that indicated sexual behaviour were;

- Number of sexual acts with partners during the previous month.
- Number of sexual acts in which condoms were used in the previous month.
- Diagnosis of a sexually transmitted infection.
- Diagnosis of pregnancy based on self report and urinary pregnancy test in female participants.

7.8 Field management

The trial was conducted in a clinic setting and participants were interviewed, treated and counselled in the same place. Research procedures were followed strictly as per protocol.

All interviews were conducted in isiXhosa.

7.9 Quality Control

7.9.1 Improvement of Validity

Partners in a couple were interviewed separately for privacy and confidentiality in order to encourage honest answers.

Interviewer sex was matched with that of the respondent for respondents to feel at ease while giving information.

7.9.2 Improvement of Reliability

Reliability was improved by training of interviewers so that questions were asked in the same way for all respondents.

Test re-test method was used in the questionnaire. This method asked the same or connected questions in different ways to help interviewer ascertain if similar answers were given by respondent.

7.9.3 Pilot Study

The study was piloted to ensure respondents understood the questions and to gauge the amount of time required for questionnaire administration.

8.0 DATA MANAGEMENT AND ANALYSIS

Data will be exported, managed and analysed using STATA version 10.1 ⁽³⁰⁾. Univariate, bivariate and multivariate associations will be explored before any further analysis is done.

8.1 Sexual behaviour

We will define protected sexual acts as those acts in which the index participants report condom use. Change in sexual behaviour as measured by incidence of protected sexual acts reported by index participants at baseline and at follow-up, will be compared using Poisson mixed effect models where total number of sexual acts will be the exposure variable. These models rely on model-based imputation through maximum likelihoods and thus reduce bias from loss to follow-up. The possible predictors of protected sexual acts in addition to time (baseline versus follow up), will include demographic and personal characteristics, as well as laboratory measurements such as CD4 cell count. Several models will be investigated by successively adding risk factors to smaller models in a logical stepwise manner. All models will be compared with Aikake's Information Criterion (AIC) statistics and the final model with the lowest AIC will be chosen. Interaction terms will be created between the risk factors in the final model if it is believed that effect modification may occur by some variables. They will be added to the model one at a time and their significance checked at 5% level. An interaction term will be added to the model only if it makes a significant contribution to the model, lowers the AIC appreciably and if we have prior knowledge of how it could be associated with condom use.

8.2 Pregnancy

Pregnancy after enrolment will be an indicator of a sexual encounter without the use of condoms. The analysis will be restricted to female index participants of child bearing age (15 to 49yrs). Descriptive characteristics comparing the women who got pregnant and those who did not will be explored. The Kaplan Meier method will be used to analyse and illustrate incidence of pregnancy and time to pregnancy. The date of the last menstrual period was collected for every pregnant index participant. Survival time for those who became pregnant during the one year (uncensored observations) will be from consent date to date of last

normal menstrual period. Survival time for those who did not become pregnant during the one year (censored observations) will be from consent date to their respective last follow up date.

8.3 Genital tract infections

Prevalence of genital tract infections among female index participants will be summarised by calculating the ratio of participants with infection over the total number of participants at baseline and at follow up months 3, 6, 9 and 12. Chi-square test for trend will be used to test for any trend in prevalence of genital infections with time.

8.4 Validity of sexual behaviour

The total sexual acts and frequency of protected sexual acts by use of condoms reported by index participants will be checked against those reported by partner participants for validity. Percentage of agreement between index and partner participant responses on these variables will be generated using Wilcoxon signed rank test.

9.0 STUDY LIMITATIONS

This is a secondary data analysis so its validity is dependent on the validity of the primary study. This study will rely on self reported sexual behaviour which is prone to social desirability bias yet it was not validated by any other method such as for biological markers in the primary study. Recall bias could also bias the sexual behaviour information.

10.0 ETHICS AND COMMUNICATIONS

All data for the secondary analysis was provided with no patient identifiers. Confidentiality was kept during the trial. Written informed consent was obtained from each study participant prior to both screening and enrolment.

Participants were compensated for their time and effort and reimbursed for costs associated with travel to the study site, time away from work and childcare. Participants were able to withdraw from the study at any time if they so wished.

10.1 Potential Harms

There will be no potential harm as a result of this secondary analysis of the data.

10.2 Potential benefits

The results of this study will be used to inform HIV prevention and policy on counselling of heterosexual HIV discordant couples. The study findings will be used as a stepping stone in the planning and management of HIV discordant couples who have emerged as a high risk group for HIV transmission in Africa. It will add to the body of knowledge around sexual behaviour of HIV discordant couples.

10.3 Results and communication

The results of this study will be published with permission from the authors of the prevention trial with the hope that it will inform policy. All results will be provided to the Department of Health, Provincial Government of Western Cape.

11.0 LOGISTICS

11.1 Budget

This is a secondary analysis so costs incurred will not be major.

11.2 Time line

Year	2010												2011	
Months	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Activity														
Protocol development														
Protocol submission for approval														
Literature review														
Data analysis														
Results														
Discussion														
Write up														
Journal manuscript														

Months of the year 1 to 12, represent months January to December 2010.

Month 13 and 14 represent months January and February 2011.

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(30) Stata Corporation, 4905 Lakeway Drive, College Station, Texas 77845 USA.

University of Cape Town

PART B: STRUCTURED LITERATURE REVIEW

1.0 INTRODUCTION

1.1 Objective

The objective of this literature review will be to summarise evidence for the existence of HIV discordance in Africa and factors influencing HIV transmission among heterosexual HIV discordant couples. Studies on effectiveness of condoms and prevalence of condom use among these couples will be highlighted. Predictors of condom use as well as measurement of condom use will be discussed further. Lastly a summary of studies on effects of HIV testing and counselling on sexual behaviour and validity of sexual behaviour will be presented.

1.2 Search strategy

Studies on heterosexual HIV discordant couples were identified by searching PubMed, Google Scholar, Science Direct and Cochrane library for studies published between 1991 and 2010. Studies with relevant key words in their titles were identified from reference lists of selected studies. Both quantitative and qualitative studies among heterosexual HIV discordant couples were selected if they contributed to attaining the goals of the literature review.

Search terms included; “HIV discordancy”, “HIV discordance”, “HIV discordant couples”, “HIV discordant partners”, “HIV transmission discordant couples”, “HIV transmission discordant partners”, “condom use” “condom usage”, “effectiveness HIV testing counselling sexual behaviour”, “sexual behaviour change VCT”, “effect VCT sexual behaviour “validity sexual behaviour” and “validity reported condom use.”

1.3 Quality and relevance criteria of included studies

Studies from both developing countries and developed countries were included in the literature review. Most of the articles retrieved were published in peer reviewed journals but grey literature from conference proceedings was also included.

Systematic reviews of randomised control trials (RCTs), before and after studies as well as cohort studies were included for the evidence on effects of HIV testing and counselling on sexual behaviour as these had the advantage of synthesizing and summarising most available evidence on this topic. Observational studies on factors influencing HIV transmission among HIV discordant couples and validity of reported sexual behaviour were included.

Cross-sectional, cohort, before and after studies, systematic reviews and qualitative studies evaluating evidence on prevalence and effectiveness of condom use among heterosexual HIV discordant couples were included. Qualitative studies were more appropriate in determining perceptions than quantitative studies and hence were included.

2.0 LITERATURE

2.1 HIV Discordance in Africa

HIV discordance refers to a situation in which only one member of a sexual partnership is HIV infected ⁽¹⁾. There were regional differences in prevalence of HIV discordance. In Eastern and Southern Africa, HIV discordance ranged from 36% to 85% with an overall rate of 49% ⁽²⁾. In South Africa the prevalence of HIV discordance was 27% in 2008 ⁽²⁾. This was the only study on HIV discordant couples identified in South Africa.

In a nationally representative HIV/AIDS Sero-Behavioural Survey among adults (15 to 59 years of age) in Uganda, 40% of cohabiting couples were HIV discordant ⁽³⁾. An HIV status evaluation of household members of HIV infected patients in a home-based ART care project

in Uganda, revealed that 52 (43%) of the spouses of the 120 participants on ART, were HIV-negative. Ninety nine percent of these spouses had never been tested before and were therefore unaware of their HIV discordant status ⁽⁴⁾.

Similarly a review of standard demographic and health surveys to describe HIV infection among couples in five Eastern and Western African countries (Tanzania, Kenya, Burkina Faso, Cameroon and Ghana), revealed that two-thirds of HIV-infected couples were discordant and one-third were concordant positive ⁽⁵⁾. Women were the infected partner in 30 to 40% of discordant relationships in these countries. In other studies among HIV discordant couples, men were as likely as women to be the HIV infected partner ^(6,7).

There is an urgent need for interventions targeting HIV discordant couples for HIV prevention and a need to assess the effectiveness of these interventions. A critical look at factors that influence HIV transmission among heterosexual HIV discordant couples could inform HIV prevention strategies among these couples.

2.2 Factors influencing HIV transmission

The transmission of HIV infection among adults in sub-Saharan Africa is predominantly heterosexual ⁽⁸⁾. Studies confirm that a substantial proportion of these heterosexual transmissions occur among HIV discordant couples ^(6,9-11). For instance in Lusaka, Zambia and Kigali, Rwanda, a base model that assumed 20% of HIV discordant relationships result in HIV transmission in each 12 month period, estimated that 55% to 93 % of new heterosexually acquired HIV infections among adults in urban Zambia and Rwanda occurred within HIV discordant marital or cohabiting relationships ⁽¹⁰⁾.

A number of factors have been shown to modify the risk of transmission of HIV within discordant couples. Persons with advanced clinical stage, low CD4 cell count and high viral load were more likely to transmit the virus to their HIV-negative partners ^(12,13).

The higher the frequency of sexual contact within HIV-discordant couples, the higher the probability of HIV transmission. The risk of HIV transmission from men to women was higher than from women to men ^(6,14,15). Besides the sex of the uninfected partner, the more sexual partners with whom a person has unprotected sex with, the higher the risk of exposure to HIV infection ⁽¹⁶⁾.

Partner overlap or concurrency increased the risk of HIV transmission ⁽¹⁷⁾. Concurrency amplifies transmission because “it exposes multiple partners to the risk of HIV infection and thereby creates a potentially large sexual network through which HIV circulates extensively” ⁽¹⁸⁾. Furthermore concurrency increases the risk of spread of other sexually transmitted infections among members of a sexual network.

Genital tract infections including STIs in both HIV-positive and negative individuals are associated with increased risks of HIV seroconversion ⁽¹⁹⁾. These infections enhance transmission and acquisition of HIV. Genital tract infections increase shedding of the virus in the genital tract increasing the probability of transmission from the HIV infected individual. Genital tract infection and in particular sexually transmitted infections in the HIV-uninfected partner cause ulcers or inflammation which increase susceptibility to HIV ⁽²⁰⁾. Ulcerative STIs breach mucosal surfaces facilitating transmission and acquisition of HIV ⁽²¹⁾.

Prevention strategies such as the ABC (abstinence, be faithful, condom use) ⁽²²⁾, antiretroviral therapy, VCT and education on transmission risks ⁽²³⁻²⁵⁾, reduce HIV transmission. Condom use is one of the strategies recommended for prevention of HIV transmission among heterosexual couples ⁽²⁶⁾.

2.4 Prevalence and effectiveness of condom use

Condom promotion strategies have been widely implemented in Africa to reduce the transmission of HIV. A longitudinal study of 343 HIV-negative steady partners of HIV infected men indicated that the use of condoms during every sexual encounter was associated with a 90% reduction in risk of HIV transmission ⁽²⁷⁾. In a European multi-country prospective study among HIV discordant couples to determine transmission of HIV to negative partners, half of the couples reported using condoms at every intercourse and no HIV transmission occurred among these couples ⁽²⁸⁾. In a Haitian HIV discordant couples study, among the 177 couples (37%) who remained sexually active after enrolment, the HIV seroconversion rate was 5.4 per 100 person year. The infection rate was 1.0 per 100 person years among those who reported that they always used condoms (2.4% of 42 couples), compared with 6.8 per 100 person years among those who used condoms inconsistently or not at all ⁽²⁹⁾.

A Cochrane review to estimate condom effectiveness in reducing heterosexual transmission of HIV concluded that consistent use of male condoms resulted in an 80% reduction in HIV incidence ⁽³⁰⁾. Consistency was defined as using a condom for every act of penetrative vaginal intercourse. The reduction in HIV risk with condom use was found to range between 90% and 95% in another review ⁽³¹⁾.

In a review of prospective studies on effectiveness of condoms in preventing STIs besides HIV, it was concluded that condoms protect against these infections ⁽³²⁾. In this review, using condoms during more than 25% of sexual acts was associated with a 92% reduction in the risk of women acquiring HSV-2 but was not protective among men. Women who reported consistent condom use had a 62% reduction in risk of acquiring gonorrhoea and a 26% reduction in risk of acquiring Chlamydia infection.

In a qualitative study on knowledge and challenges of HIV prevention amongst discordant couples in Uganda, condom use was reported as the preferred prevention strategy for HIV transmission. A number of couples transitioned to condom use after failing to abstain or reduce their frequency of sex ⁽²⁶⁾.

The prevalence of condom use among HIV discordant couples has been found to be low in African studies prior to any intervention ⁽²³⁻²⁵⁾. In studies enrolling HIV discordant couples, condom use prior to HIV testing and counselling was 4% in Kigali, Rwanda ⁽²³⁾ and 3% in Lusaka, Zambia ⁽²⁵⁾.

A prospective cohort study conducted on the probability of HIV transmission in monogamous heterosexual HIV-1 discordant couples in Rakai, Uganda revealed that self reported condom use was low in the 174 monogamous couples despite the fact that condoms and counselling were promoted and offered free of charge during the study ⁽³³⁾. All the couples were married or cohabiting and 161 (92%) had never used condoms, 11 (6%) reported occasional condom use and only 2 (1%) reported consistent condom use.

In a study on HIV serodiscordant couples diagnosed in a referral hospital in Thailand, seroconversion occurred in couples who did not consistently use condoms. A higher proportion of those who seroconverted reported having sex without condoms (75%) compared to those who remained seronegative (37%) though this was not statistically significant, ($p=0.14$) ⁽³⁴⁾.

An HIV/AIDS Sero-Behavioural Survey among adults in Uganda found that participants who knew their HIV status were 3 times more likely to use a condom at last sexual encounter compared to untested participants while those who knew their partner's HIV status were 2.3 times more likely to use condoms at last sexual encounter compared to those unaware of their partner's status ⁽³⁾. This suggests that there is a role for HIV testing and counselling strategies

among couples. There were no RCTs on effectiveness of condom use in prevention of STIs because this would be un-ethical given the proven effectiveness of condoms.

2.4.1 Predictors of condom use

A number of factors were found to be associated with condom use among HIV discordant couples. In the California Partners Study of heterosexual HIV discordant couples, multivariate analyses showed that inconsistent condom use was associated with injection drug use, with younger HIV-positive partner (less than 40 years of age) (OR= 4.8, 95% CI 1.0-22.6) but not in couples with an older HIV-positive partner (OR= 0.3, 95% CI 0.1-1.4)⁽³⁵⁾. African-American couples reported more inconsistent condom use compared to other races (Hispanic, White, Native American, Asian and other). Couples who practiced anal sex, couples with male bisexual HIV-positive partners and those with HIV-positive partners with a lower CD4 cell count, were more likely to have unprotected sex⁽³⁵⁾.

In the univariate analysis, inconsistent condom use was associated with; unemployment, lower education, injection drug and cocaine use level, practice of anal sex, positive partner not receiving ART and higher CD4 cell count of HIV-positive partner in HIV discordant heterosexual couples⁽³⁵⁾. In this study unemployment was defined as none of the partners earning an income while low education (having attained high school graduation or less), drug use and practice of anal sex was defined as such if one or both partners had the characteristic.

A study on HIV transmission among HIV discordant couples in rural Uganda revealed that HIV-negative men with infected partners reported more frequent condom use (17%) than HIV-positive men with uninfected partners (10%), $p < 0.05$ ⁽³⁶⁾.

One of the factors influencing the consistent use of condoms by heterosexual HIV discordant couples is the desire to have children. This desire to procreate may be one of the reasons for

the persistent HIV incidence among HIV-discordant couples in Africa and other parts of the world ⁽²³⁾.

In an exploratory study assessing sexual health, reproductive desires and strategies for preventing HIV transmission among HIV discordant couples in long-term relationships in South Africa and Tanzania, 51% of couples desired children. The need to avoid infecting the HIV-negative partner often conflicted with the desire for children. Sixty percent of participants reported that intimacy had been affected by their discordant relationship, with changes in sexual relations due to fear of infecting the negative partner and the need for condom use ⁽¹¹⁾.

In a study to determine the effect of an HIV counselling programme on rates of HIV infection and pregnancy in 178 married heterosexual HIV discordant couples in Kinshasa, Democratic Republic of Congo, couples seeking to have children minimized their risk of transmission by having unprotected sex only during the woman's perceived monthly ovulatory period, indicating that despite the couples' desire to have children they understood the risk of transmission to the negative partner and limited unprotected sex. . The overall risk of HIV transmission per sexual act was 0.0011 (95% CI 0.0008 – 0.0015) among monogamous heterosexual HIV discordant couples in Rakai, Uganda ⁽³⁷⁾ .

2.4.2 Condom use measurement

The measurement of condom use was conducted in various studies on sexual behaviour ^(23,24,29,34). It was suggested from reviews that continuous measures of condom use were superior to dichotomous measures ⁽³⁸⁾. Continuous measures encouraged more honest answers as they made respondents feel that it was normal and expected by the interviewer that they did not use condoms during every previous sexual act ⁽³⁹⁾. Furthermore continuous measures gave more statistical power during analysis.

Recall periods of less than 3 months were more likely to give more accurate results ^(38,40). It was found that it was important to specify variables related to condom use including partner type and type of sex act as these made the resulting data more meaningful ⁽⁴⁰⁾. This was because there may be differences in rates of condom use between main and casual partners and for anal or vaginal sex. Specifying the types of participants and nature of sex allowed more meaningful interpretations of studies ⁽⁴¹⁾.

2.5 Effects of HIV testing and counselling on sexual behaviour

A number of studies have shown that there was an increase in self reported use of condoms by heterosexual HIV discordant couples following confidential HIV testing and counselling ^(23-25,42,43). In a prospective study of 60 HIV discordant couples in Kigali, Rwanda, the proportion of discordant couples using condoms after HIV testing and counselling increased from 4% to 57% after one year of follow up, $p < 0.05$ ⁽²⁴⁾.

Following voluntary counselling and testing at a VCT centre in Lusaka, Zambia, more than 80% of reported sexual acts among 963 cohabiting heterosexual discordant couples included condoms after VCT compared to less than 3% prior to VCT, $p < 0.05$ ⁽²³⁾.

As part of a longitudinal study, husbands and cohabiting partners of 648 Rwandan women were recruited in a male-focused HIV counselling programme in Rwanda, Kigali. All women and 37% of the men had previously received VCT services. A condom ratio (number of acts of penetrative sex with condoms as a proportion of the total number of sex acts) was used. Regular condom users were couples in whom both partners independently reported condom use resulting in a condom ratio that exceeded 0.9. The proportion of couples who qualified as regular condom users increased from 5% to 65% among the HIV discordant couples at the end of one year, $p < 0.05$ ⁽²⁵⁾.

A systematic review that included a meta-analysis on effects of HIV testing and counselling on sexual behaviour was done on studies conducted between 1985 and 1997 ⁽⁴³⁾. This review concluded that after HIV testing and counselling, HIV-positive participants and HIV discordant couples increased condom use more than HIV-negative and untested participants. The weighted mean effect size of condom use among the serodiscordant couples was $d = 1.31$ (95% CI = 1.14 – 1.48, Q statistic = 147.43, $p < 0.001$) and studies were homogenous. In this study the standardised mean difference index (d) was used and positive effect sizes indicated reductions in risky sexual behaviour ⁽⁴³⁾. An effect size of ± 0.2 was considered small and above ± 0.8 was large ⁽⁴⁴⁾.

Another systematic review and meta-analysis on effectiveness of behavioural interventions in developing countries included studies conducted between 1990 and 2006 ⁽⁴²⁾. Three of the studies measured condom use following HIV counselling and testing among HIV discordant couples. Pooled data from these studies ($n = 312$) showed condom use increased (OR: 67.38; 95% CI: 36.17–125.52). The Q statistic of 0.96 showed no statistically significant heterogeneity ($p = 0.62$; $I^2 = 0.000$) across these three studies.

Only one prevention trial on the effectiveness of HIV testing and counselling was identified in Africa. Voluntary counselling and testing was associated with a reduction in incidence of sexually transmitted infections in this randomised control trial in Kenya ⁽⁴⁵⁾. Respondents who reported unprotected sexual intercourse with non-primary partners were twice as likely to have an incident STI compared to those not reporting unprotected sex with non-primary partners, $p = 0.01$. Those who reported unprotected sex at baseline were twice as likely as those who did not report this to have an incident STI, $p < 0.025$, after adjusting for unprotected sex with non-primary partner at 6 months.

Studies on the effectiveness of HIV testing and counselling as part of HIV prevention trials were limited. There is a need for further research on whether couple counselling is more effective and beneficial compared to individual counselling among heterosexual HIV discordant couples, including specially designed counselling strategies to help heterosexual HIV discordant couples cope with their serostatus and prevent transmission of the virus to their HIV-negative partner and others.

2.6 Validity of self reported sexual behaviour

Sexual behaviour is subject to varying degrees of social, cultural, religious, moral and legal norms and constraints. Therefore a key challenge of all research using self reported sexual behaviour is the generation of unbiased and precise results ⁽⁴⁶⁾.

Validity describes the extent to which an instrument or tool accurately measures what it purports to measure. It is extremely difficult to determine the validity of self reported sexual behaviour and therefore a number of indirect methods are used. These methods can use external or internal validation ⁽⁴⁶⁾.

The internal consistency of questionnaire responses is checked by looking for agreement of related questions in the questionnaire and the use of two or more data collection tools to collect similar information from the same participants ⁽⁴⁶⁾. In a nationally representative survey of sexual behaviour in Britain (Natsal study), 19,000 adults aged 16 to 59 years were interviewed using face to face interviews and were also asked to complete self-administered questionnaires. Answers to particular questions were compared for consistency by the two methods. There were 185 consistency checks and 80% of respondents had no inconsistencies. However the single most frequent inconsistency was reporting one sexual partner ever in the interview and two or more in the self completion questionnaire ⁽⁴⁷⁾.

External validation of reports may be achieved by using independent data sources as external references ⁽⁴⁶⁾. In the Natsal survey, percentage of self reported therapeutic abortions was compared to national reports and was found to be similar. When self reports of having sought treatment for past STI symptoms were compared with STI clinic records, there was evidence of under-reporting of STI clinic attendance by respondents ⁽⁴⁸⁾.

Interviewing of respondents and their sexual partners separately has been used to test external validity ⁽⁴⁹⁾. Individual responses differed depending on the stability of the relationship, degree of substance abuse and the duration of reporting period ⁽⁵⁰⁾. High levels of agreement were found in a ten year study on risk factors for HIV transmission among HIV discordant couples. The risk factors included frequency of sex, practice of anal sex and reports of unprotected sex ⁽⁵¹⁾.

Biological methods such as urinary testing for HIV, *Chlamydia trachomatis* and pregnancy were used to assess the validity of self reports on sexual behaviour ⁽⁴⁶⁾. It was hypothesized that lower STI incidences would be found in persons who reported consistent condom use ⁽⁵²⁾. There was no difference in incident STIs between STI clinic attendees who reported having always used condoms and those who never used condoms at all, suggesting reporting bias. At follow up 15.3% of respondents had STIs in both groups.

When self reported sexual behaviour among HIV discordant couples was validated with biological markers there was evidence of under-reporting ⁽²³⁾. Sperm on vaginal swabs, pregnancy and linked HIV transmission were used to validate reported protected sex within couples. Sperm was present in 25% of vaginal smears taken in intervals with reported unprotected sex compared with 15% of smears taken when no unprotected sex was reported [$P < 0.001$]. The detection of sperm in intervals of no reported unprotected sex confirmed under-reporting ⁽²³⁾. Two percent of intervals with no reported unprotected sex were

associated with pregnancy while linked HIV transmission was confirmed in 3% of intervals with no reported unprotected sex. Linked HIV transmission was confirmed using molecular epidemiology⁽²³⁾.

In the same study diagnoses of incident episodes of gonorrhoea, syphilis and *Trichomonas vaginalis* were used to validate self report of extra-marital sexual contact. Incidence was lower when there were no reported outside sexual contacts by couples compared to when outside contacts were reported. The fact that these infections were diagnosed in intervals of no reported outside sexual contacts confirmed reporting bias⁽²³⁾.

Conclusion

Heterosexual transmission is an important route of HIV transmission. Given the high rates of HIV discordance in South Africa and the region it is important to determine the effects of HIV prevention strategies among HIV discordant couples. Studies among HIV discordant couples including those determining the effectiveness of VCT among heterosexual HIV discordant couples enrolled as part of prevention trials are limited.

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PART C: JOURNAL MANUSCRIPT

AIDS and Behavior journal

**EFFECT OF COUNSELLING EDUCATION AND CONDOM PROVISION ON
SEXUAL BEHAVIOUR OF HETEROSEXUAL HIV DISCORDANT COUPLES**

***Running Head: Effect of counselling on sexual behaviour heterosexual HIV discordant
couples***

Dr Phiona Enid Namale^{1,4,5} Dr David Coetzee^{1,2,4,5} A/Prof Francesca Little^{3,4,5}

Correspondence author: Dr Phiona Enid Namale

15 Dunvegan Gardens Hope Road Rose Bank 7700 Cape Town Tel: +27 791 966 460

Email: phnamale@yahoo.com

School of Public Health & Family Medicine¹ Department of Infectious Diseases² Department
of Statistical Sciences³ University of Cape Town⁴ Cape Town South Africa⁵

EFFECT OF COUNSELLING AND CONDOM PROVISION ON SEXUAL BEHAVIOUR OF HETEROSEXUAL HIV DISCORDANT COUPLES ENROLLED IN AN HIV PREVENTION TRIAL SOUTH AFRICA

Phiona Enid Namale. David Coetzee. Francesca Little.

Abstract

Studies have been conducted among HIV high risk groups in South Africa to improve HIV prevention. A prevention trial to assess efficacy of daily acyclovir on HIV transmission among heterosexual HIV discordant couples was conducted in South Africa. HIV counselling and condoms were offered to these couples and self reported information on sexual behaviour collected. The objective of this study was to examine the effect of counselling and condom provision on sexual behaviour of these couples. At the end of one year, the incidence rate ratio of protected sexual acts among couples was 50% higher than at baseline. Presence of non-primary partners among index participants and earning by the partner participant reduced the incidence rate ratio of protected sex by 25% and 6% respectively.

Counselling and condom provision offered to heterosexual HIV discordant couples as part of an HIV prevention trial resulted in an increased rate of condom use.

Key words: HIV. Discordance. Couples' counselling. Condoms

⁶ *Supplementary results have been added to the appendices and this is a variation from the journal requirements.*

INTRODUCTION

In 2007, Sub-Saharan Africa accounted for 67% of the 33 million people living with HIV/AIDS globally and Southern Africa as a region contributed 35% of this total ⁽¹⁾. The HIV epidemic in South Africa is described as hyper-endemic given that more than 15% of the adult population (15 to 49 years) are living with HIV ⁽¹⁾. In 2008, the HIV prevalence in South Africa was 16.9% (15 to 49 age group) ⁽²⁾ with an incidence of 17 per 1000 in the 15 to 20 age group. Thus there is a need for targeted HIV prevention strategies among high risk groups, such as; sex workers, men who have sex with men, intravenous drug users and HIV discordant couples.

HIV discordance refers to a situation where only one member of a sexual partnership is HIV infected ⁽³⁾. Despite being in stable or long term partnerships, high rates of HIV transmission have been found within heterosexual HIV discordant couples who are often unaware of each other's HIV status ^(4,5). In Sub-Saharan Africa approximately 50% of HIV infected persons are in an HIV discordant relationship ⁽⁶⁾. In South Africa, the prevalence of heterosexual HIV discordance was 27% in 2008 ⁽⁷⁾ and hence they are an important group to target.

A number of studies have shown that condoms are highly effective in preventing HIV transmission ⁽⁸⁻¹¹⁾. Prevalence of condom use among HIV discordant couples was less than 10% prior to any intervention in African studies ⁽¹²⁻¹⁴⁾.

Only one prevention trial on effectiveness of HIV testing in Africa (Kenya and Tanzania) was identified ⁽¹⁵⁾. This prevention trial showed that HIV counselling and testing was superior to provision of health information only, in reducing unprotected sex among both HIV concordant and HIV discordant couples and also decreasing incidences of sexually transmitted infections (STIs). Voluntary counselling and testing (VCT) also increased condom use among HIV discordant couples in other studies ^(12-14,16,17). Knowledge on effect

of counselling and condom provision among HIV discordant couples enrolled as part of HIV prevention trials in South Africa is limited.

A number of factors modify the risk of HIV transmission. Later stage of HIV infection, lower CD4 cell count and high viral loads of the infected partner and STIs in either sexual partner increase transmission risk ^(18,19). Interventions such as abstinence, condom use ⁽²⁰⁾ and antiretroviral therapy ^(20,21) reduce HIV transmission risks.

In 2007/2008 a phase III placebo controlled prevention trial among heterosexual HIV discordant couples was undertaken in 12 sites in Africa to determine if suppression of *Herpes Simplex II* virus using daily acyclovir reduces HIV transmission among heterosexual HIV discordant couples. This study assessed the effect of counselling and condom provision on sexual behaviour of couples enrolled at one of the South African sites over a one year period.

METHODS

Study population

The prevention trial was conducted in the Klipfontein sub-district, Cape Town, Western Cape province of South Africa. Heterosexual HIV-discordant couples in which the HIV-infected partner (index participant), had a CD4 cell count of at least 250 cells/mm³ at screening and their uninfected primary partner (partner participant) were enrolled. Heterosexual couples were defined as sexual partners of the opposite sex who were married, were living together, or otherwise considered each other a primary partner.

Sample size calculation

Using a sign test of equality of paired proportions with a 5% two-sided level of significance, a sample size of 120 pairs had 86% power to detect a difference in proportions of 0.2 (20%) when the proportion of discordant pairs is expected to be 0.50. Allowing for 25% non-

response rate, a further 30 pairs were required giving a sample size of 150 HIV discordant couples.

Data collection

Information on sexual behaviour was collected using interviewer-assisted questionnaires. The index participants were interviewed on a monthly basis while their partners were interviewed quarterly. Couples were asked to report the total number of sexual acts and frequency of condom use in the preceding month. HIV counselling was offered at each visit and couples were counselled together quarterly. Individual counselling was offered if preferred by participants. Partners underwent HIV testing every three months. Condoms were provided to all participants at every visit. All participants were examined for and asked about symptoms of STIs. Treatment of STIs was based on clinical findings and/or laboratory confirmation. Urinary pregnancy tests were performed on the female participants quarterly or when pregnancy was suspected.

Data Analysis

Data was exported, managed and analysed using STATA version 10.1⁽²²⁾.

Sexual behaviour

Change in sexual behaviour as measured by incidence of protected sexual acts reported by index participants at baseline and at follow-up was compared using Poisson mixed effect models where total number of sexual acts was the exposure variable. These Poisson models relied on imputation through maximum likelihoods so reduced bias from loss to follow-up. Other predictors of protected sexual acts included demographic and personal characteristics, as well as laboratory measurements such as CD4 cell count. Several models were investigated by successively adding risk factors to smaller models in a logical stepwise manner. All

models were compared with Aikake's Information Criterion (AIC) statistics and the final model with the lowest AIC was chosen.

Validity of self reported sexual behaviour

The frequency of protected sexual acts and total number of sexual acts as reported by index participants were checked against those reported by partner participants for validity. Percentage of agreement between index and partner participant responses on these variables was generated using the Wilcoxon signed rank test.

Pregnancy

The analysis was restricted to female index participants of child bearing age (15 to 49 years). Descriptive characteristics comparing the women who got pregnant and those who did not were explored. The Kaplan Meier method was used to analyse and illustrate incidence of pregnancy and time to pregnancy.

Genital tract infections

The prevalence of genital tract infections among index participants was summarised by calculating the ratio of participants with infection over the total number of participants at baseline and at follow up months 3, 6, 9 and 12. Chi-square test for trend was used to show the trend in prevalence of genital infections over time.

RESULTS

Ninety two (47%) of couples attended all 12 follow-up visits (numbers who attended each visit showed in appendix). Index and partner participants lost to follow-up at 12 months were not significantly different from those who attended all visits except for age (tables comparing characteristics shown in appendix). Table I summarises the baseline characteristics of all study participants. Index and partner participants had differences in age, years of school,

number earning and percentage of both sexes. Of the 196 index participants enrolled, 79% (154) were women and 21% men. The mean age was lower in index participants, 34years (C.I 32.4–35.02) compared with partner participants, 37years (35.16–37.89), ($p < 0.001$ Paired t-test). More partner participants than index earned an income, ($p = 0.01$, Paired t-test). Index participants had more years of schooling than partner participants, ($p = 0.03$ Paired t-test). At baseline, 6 (3%) of the index participants had other partners while none of the partners reported other partners. At follow-up, 7 (4%) of index participants reported having other partners and none were reported by partners.

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Table I: Baseline and demographic characteristics of heterosexual HIV discordant couples

	Index participants	Partner participants
	n=196	n=196
Characteristic	Mean (Se)	Mean (Se)
Age	33.7 (0.66)	36.5 (0.69)
Years in school	8.92 (0.19)	8.38 (0.20)
Characteristic	Frequency (%)	Frequency (%)
Females	154 (79)	42 (21)
Married to study partner	29 (15)	31 (16)
Living with study partner	119 (61)	126 (64)
Number earning an income	44 (22)	64 (33)
Resident in formal settlement	98 (50)	107 (55)
<i>n (number of participants) Se (Standard error) % (Percentage)</i>		

Less index participants reported being married to their study partner compared to reports from partner participants, 29 compared to 31. Less index participants reported living with their study partner compared to partner participants. This is an indication of discrepancy among couple responses as same responses would be expected within couples, as each index participant was enrolled with one primary partner participant.

Condom use

Among all participants regardless of number of visits attended, the mean proportions of protected sex at follow up were significantly higher than those at baseline, 0.96 (C.I 0.92–1.00) and 0.71 (C.I 0.65–0.77) respectively (box and whisker plot shown in appendix). Among those who attended all study visits, the mean proportions of protected sex at follow up were significantly higher than those at baseline, 0.93 (C.I 0.88–0.97) and 0.63 (C.I 0.54–0.73) respectively. Table II summarises the associations between protected sexual acts and different predictors (model building strategy shown in appendix). There was a 50% increased incidence rate-ratio of protected sexual acts by couples at follow-up compared to baseline. If the index participant reported other partners, the incidence rate ratio of protected sex among couples reduced by 25%. Earning by partners reduced the incidence rate ratio of protected sex among couples by 6%. This plot of observed against predicted sum of number of times condoms were used by model showed a good fit (graph shown in appendix).

Table II: Predictors of protected sexual events among all couples

Variable	Unadjusted risk	95% CI	Adjusted risk	95% CI
n=196	ratios		ratios	
Time (follow up versus baseline)	1.49	1.38 – 1.62	1.51	1.39 – 1.63
Presence of other partners among index participant (yes/no)	0.81	0.68 – 0.97	0.75	0.63 – 0.90
Partner earning (yes/no)	0.94	0.89 – 1.01	0.94	0.89 – 1.00
<i>n (number of participants)</i>	<i>95% C.I (Confidence interval)</i>			

Table.III shows the incidence rate ratios in only those who attended all study visits. There was a greater increase in incidence risk ratio of protected sex at follow-up compared to baseline among couples whose index participant attended all study visits. There was a 74% increase in the incidence rate ratio of protected sexual acts among couples who attended all visits at follow-up compared to baseline. Comparing models in table II and table III, the effect of time was lower in the model for all participants (table II), there was not much difference for presence of other partners by index participant but earning by partner is non-significant in table III.

Age and sex of participants, earning by index participants, living with study partner, marriage to study partner, types of settlement, years of schooling by participants and CD4 cell count of index participants did not enter the chosen model.

Table III: Predictors of protected sexual events among couples who attended all study visits

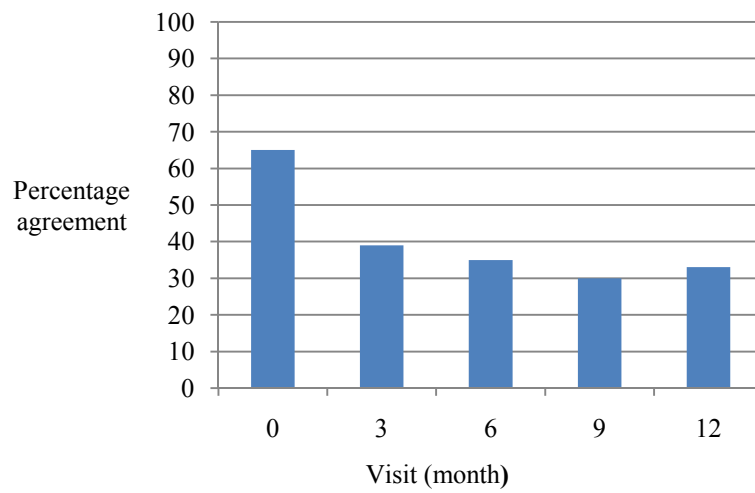
Variable	Unadjusted risk ratios	95% CI	Adjusted risk ratios	95% CI
n=92				
Time (follow up versus baseline)	1.72	1.53 – 1.94	1.74	1.55 – 1.96
Presence of other partners (yes/no)	0.78	0.62 – 1.00	0.69	0.55 – 0.86
Partner earning (yes/no)	0.93	0.84 – 1.03	0.92	0.84 – 1.01
<i>n (number of participants)</i>		<i>95% CI (Confidence Interval)</i>		

Validity of self reported condom use

Index and partner participants gave similar responses more often at baseline compared with follow-up with respect to frequency of condom use and total sexual acts. Figure 1 and figure 2 show the percentage agreement among couples. With regards to frequency of condom use and total sexual acts, 65% of couples agreed at baseline. This agreement decreased over time and was about 30% at the end of one year.

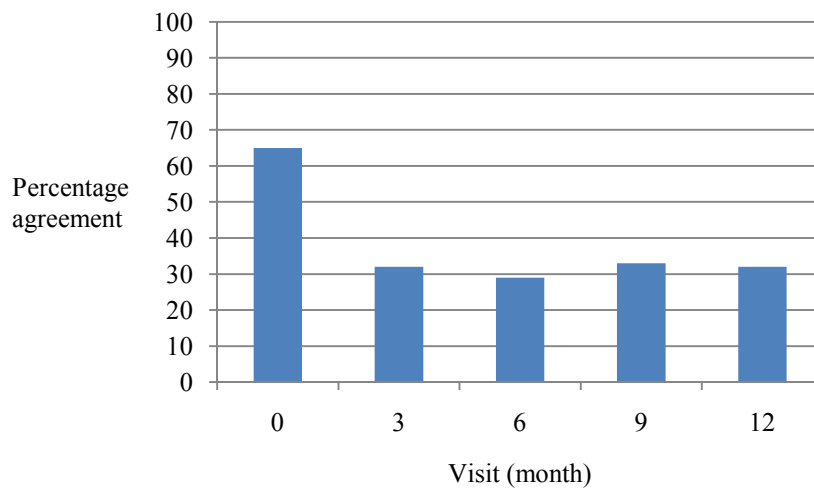
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Figure1: Percentage agreement of reported condom frequency by couples with time.



The percentage agreement of reported condom frequency among couples decreased with time.

Figure 2: Percentage agreement of reported sexual frequency by couples with time.



The percentage agreement of reported sexual frequency among couples decreased with time.

The median difference in reported condom use at follow up was zero (0) inter-quartile range (IQR) (-1 to 1). The median difference in reported sexual acts at follow-up was zero (0) IQR (-1 to 2).

Pregnancy

There were more female index participants enrolled in the trial 154 (79%). Four of these women were not of reproductive age and were thus excluded from the analysis of time to pregnancy. Ten (6%) women got pregnant during the one year of follow up.

Table IV shows the characteristics of the female index participants of reproductive age and those who got pregnant. Those who got pregnant were similar to those who did not in all characteristics except for age and type of settlement. The mean age was lower in those who got pregnant, 25 years (se =1.88, C.I 22-30) compared with 32 years (se = 4.14 CI 31-34) in those who did not. There were 2.02 pregnancies per 10000/year using Kaplan Meier analysis of time to pregnancy (graph shown in appendix).

Table IV: Distributions of characteristics among female index participants of reproductive age and those who got pregnant

Characteristic	All females n=150 Frequency (% ^a)	Got pregnant n=10 Frequency (% ^b)	p value ^c (Fischer's exact test)
Married to partner	18 (12%)	3 (17%)	0.10
Not married to partner	132(88%)	7 (5%)	
Lived with partner	83 (55%)	8 (10%)	0.19
Did not live with partner	67 (45%)	3 (2%)	
Earned an income	26 (17%)	0 (0%)	0.21
Did not earn income	124(83%)	10 (8%)	
Informal settlement	73 (49%)	9 (12%)	0.01
Formal settlement	77 (51%)	1 (1%)	
Had one spouse	146 (97%)	10(100%)	1.00
Had more than one spouse	4(3%)	0(0%)	

^a Percentage of the total participants with characteristic

^bPercentage of participants with characteristic who fell pregnant (row %)

^cP value for association between characteristic and pregnancy status

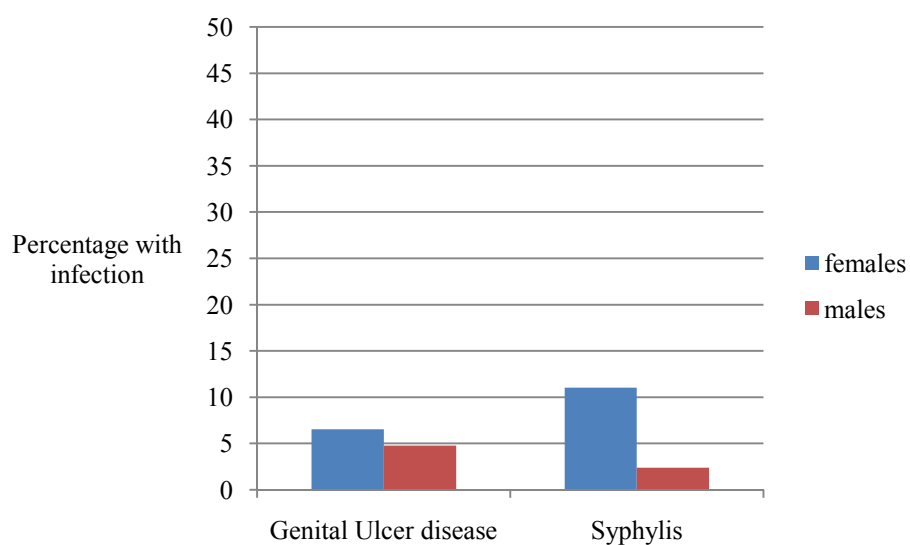
% (Percentage)

Genital tract or sexually transmitted infections

Figure 3 shows the prevalence (in percentage) of genital infections amongst all index participants at baseline and figure 4 shows the infections that affect only women. Among women, vaginitis was the commonest infection (49%) and the commonest among men was genital ulcer disease (GUD). Diagnoses of GUD included ulcers due to Herpes Simplex Virus.

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Figure 3: Genital infections among men and women at baseline



Women were diagnosed with a higher percentage of genital infections than men but this was not statistically significant, $p=0.32$ (one sided Fischer's exact test).

Figure 4: Genital infections that affect only women at baseline

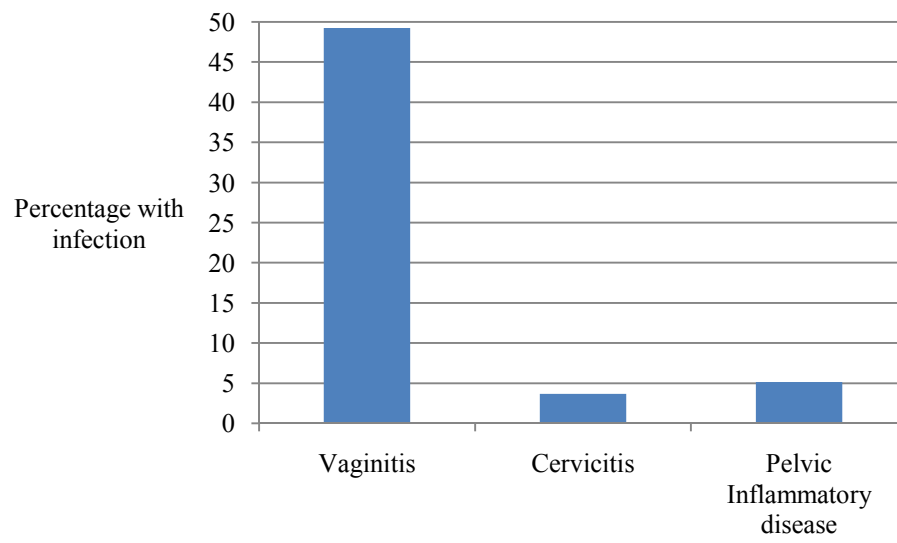
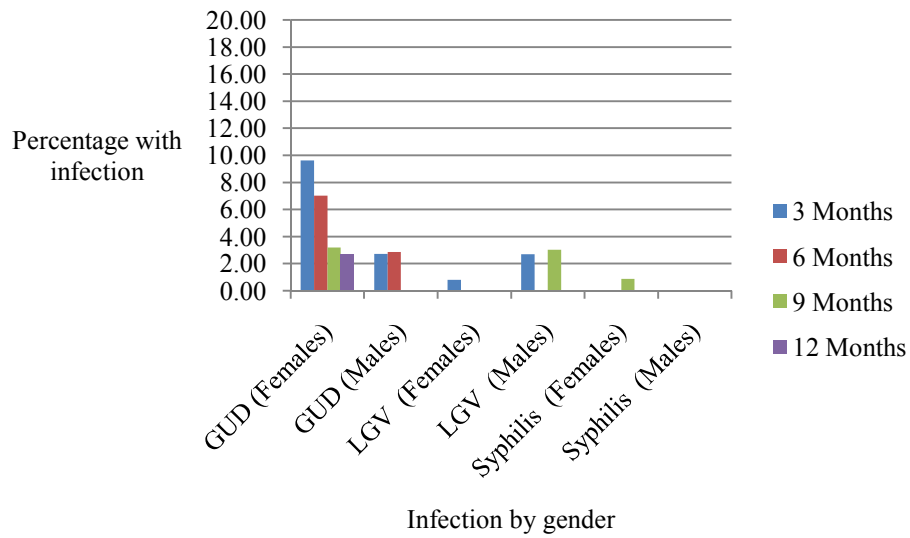


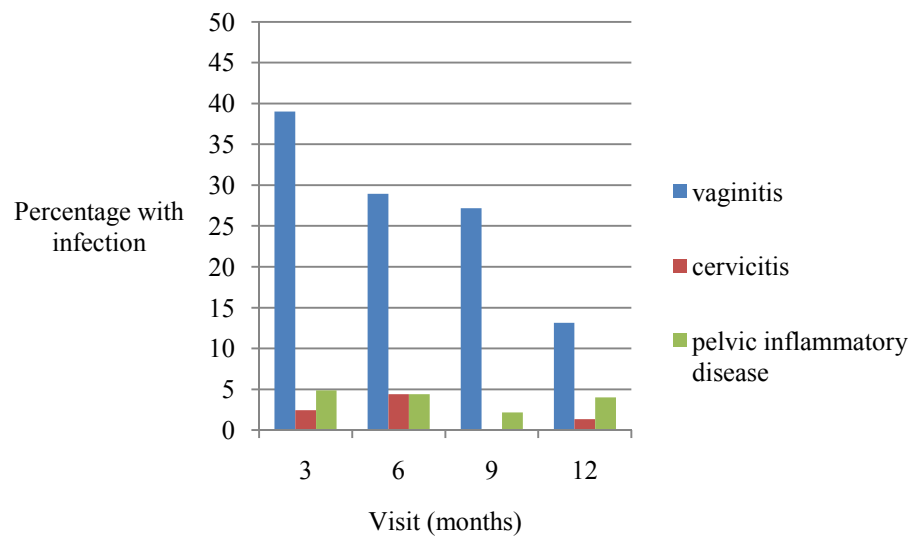
Figure 5 and figure 6 show the prevalence of infection (in percentage) among index participants at follow up. Vaginitis and GUD were still the commonest infection during follow-up (number of participants assessed for genital infections at each visit shown in appendix). Using the Chi-square test for trend, the prevalence of diagnosis of a genital tract infection decreased with time in both women and men ($p < 0.0001$) and ($p = 0.25$) respectively. None of the participants were diagnosed with urethritis, gonorrhoea, Chlamydia, bacterial vaginitis, chancroid and trichomoniasis at both baseline and follow-up.

Figure 5: Genital tract infections among men and women at follow up



There were no males diagnosed with syphilis at month 12 and syphilis was diagnosed among females at only month 9.

Figure 6: Genital tract infections that affect only women at follow up



The percentage of infections that affect only females decreased with time.

DISCUSSION

This study showed that the heterosexual HIV discordant couples enrolled in this HIV prevention trial self reported decreased unprotected sex during the trial. The rate of condom use increased over the one year period. This may have been due to the HIV counselling and the condoms that these couples received. Condom use was reported to increase among couples, who were aware of their partner's HIV serostatus ⁽²³⁾.

A similar increase in condom use among HIV discordant couples was reported in other studies after VCT for HIV ^(12,16,17,24). Unprotected sexual intercourse reduced amongst HIV discordant couples in a multicentre randomised control trial in Kenya, Tanzania and Trinidad ⁽¹⁵⁾. In this trial of 6 months duration, couple counselling was compared to provision of health information only. Unprotected sex with non-primary partner was shown to increase from 11% to 15% in the same study ($p < 0.05$). This reduction in protected sexual acts concurred with our findings of a reduction in incidence rate ratio of protected sexual acts if the index participant had other partners.

In South Africa as in most parts of Africa, societies are patriarchal ⁽²⁵⁾. This social-economic difference and power relations may explain why couples in whom partner participants earned were less likely to use condoms ⁽²⁵⁾. The majority of the partner participants were men and were more likely to be employed than their female counterparts. This male dominance coupled with the fact that women are usually not in a position to negotiate safe sex in patriarchal societies ⁽²⁶⁾ could have led to the reduction in protected sex if partners earned. However counselling and condom provision may have encouraged men's willingness to have protected sex at follow-up.

Contrary to our study results, inconsistent condom use amongst heterosexual HIV discordant couples in California was associated with unemployment and lower education level ⁽²⁷⁾.

Unemployment was defined as neither of the partners earning an income and low education was defined as one or both partners having attained high school graduation or less. In our analysis, we stratified employment by participant. Earning by index participant and education level was not significantly associated with condom use.

The lower effect of time in the model including all participants (table II) compared to model with only participants who attended all 12 follow-up visits (table III) is probably because participants lost to follow-up were less likely to have protected sex. On the other hand, the stronger effect of time among those who completed all study visits probably reflects a selection bias in that those who attended all visits were more likely to have protected sex. In the model with only index participants who completed follow-up, earning by partner was not significant probably due to the smaller sample size of 92.

The low agreement among couple responses shows that estimates of prevalence of protected sexual acts were questionable. The medians of reported total sexual acts and protected sexual acts was zero and inter-quartile ranges narrow at follow-up so relative comparisons between follow up and baseline were better than the low degree of agreement suggests as we relied on index participants' responses at both baseline and follow-up.

The prevalence of genital tract infections among index participants decreased over the visits but this decrease was significant among women only. This reduction may have been due to the prompt diagnosis and treatment of infection, counselling on risk reduction and condom use to prevent spread of infection and re-infections. This non-significant reduction of genital tract infections among men over visits may be due to the small sample size. There were only 42 male index participants and any loss to follow up made this number even smaller. The loss to follow up of participants could have biased the results by making the prevalence of genital

infections seem higher than it was by reducing the denominator (total number of participants).

Similarly VCT was associated with a reduction in incidence of STIs in a randomised control trial in Kenya ⁽²⁸⁾. In addition many studies have shown evidence of effectiveness of condoms in protection against sexually transmitted infections ^(9,11,29). The higher prevalence of genital infections among women compared with men may be due to physiological and anatomical factors such as; large surface area provided by the vagina, presence of vaginal secretions, and higher estrogen levels.

The low rate of pregnancy and decrease in prevalence of genital infections including STIs over the one year period supports the findings that rate of condom use increased over time. These incident pregnancies and genital tract infections however show lack of or inconsistent condom use among some couples. On-going counselling and support could play a vital role in maintenance of condom use.

An assessment of VCT in Kenya and Tanzania showed that it was cost effective ⁽³⁰⁾. The cost per HIV-1 infection averted was United States dollars (USD) 249 and USD346, in Kenya and Tanzania respectively. The cost per DALY saved was USD12.77 in Kenya and USD17.78 in Tanzania. In addition 1000 new HIV infections were prevented in the subsequent year in both countries ⁽³⁰⁾. The cost effectiveness of VCT may be improved by integrating couple counselling into other HIV prevention strategies and targeting high HIV prevalence areas within sub-Saharan Africa where HIV discordant relationships are a high risk group for HIV. Studies have shown that VCT is acceptable ⁽³¹⁻³⁴⁾ in Africa and has further research should identify the benefits of couples versus individual counselling and the role of support groups among HIV discordant couples. No studies have been conducted of the cost effectiveness of on-going couples' counselling.

Our findings suggest that counselling and condom provision play an important role in promoting protected sex among HIV discordant couples. However on-going support for these couples especially those who are HIV discordant is limited. Our study shows that there would be benefit of providing these interventions on an on-going basis. Group based interventions among HIV discordant couples may be useful in improving couple communication and coping mechanisms on an ongoing basis for these couples. The feasibility of such group based interventions has been shown ⁽³⁵⁾.

Couple based HIV prevention interventions have indeed shown positive effects in African studies ^(12,36-39) such as increasing condom use, disclosure rate, improving adherence to antiretroviral treatment and prevention of mother to child HIV transmission programmes. Partner participation is essential in HIV risk reduction strategies ⁽⁴⁰⁾ and may improve outcomes of these interventions. As evidenced from our findings, characteristics of both partners influenced decisions by couples to have protected sex. Presence of other partners by index participants and earning by partners reduced the incidence rate ratio of protected sex. Other studies have also shown that both partners influenced whether couples had protected sex ^(27,41,42).

The strength of this study is the fact that both individual and couple HIV counselling on HIV prevention was offered to couples and characteristics of each partner in the heterosexual HIV discordant couples was incorporated in our analysis. This allowed us to determine which characteristics of either partner played a role in determining safe sex and if this on-going counselling for a year influenced sexual behaviour. These results are generalisable to the African context where HIV discordant couples are a high HIV risk group and where already existing VCT services can incorporate on-going couple counselling for heterosexual HIV discordant couples.

Implications for research and current practice

Specially designed individual and couple counselling on prevention of HIV transmission among heterosexual HIV discordant couples is a worthwhile prevention strategy ⁽⁴¹⁾ that should be incorporated and integrated in other health services such as; family planning services, HIV testing and counselling centres, prevention of mother to child HIV transmission services and all HIV services. Issues such as; disclosure of HIV status, violence within relationships due to discordance and the decision about having children need to be incorporated into this counselling. This VCT integration should include monitoring and evaluation of outcomes such as condom usage and HIV seroconversion.

There is a need for further research into which aspects of counselling will be most useful in helping heterosexual HIV discordant couples to cope with the discordance, communication between couples including prevention of transmission to the negative partner and the general population.

Further research on cost effectiveness and benefits of on-going couple counselling as opposed to individual counselling among couples with at least one HIV-positive partner is required.

Limitations

The results of this study should be interpreted in light of its methodological limitations. This was a secondary data analysis so study validity depended on the primary study. The self reported sexual behaviour was not validated by any other method during the primary study for example, biological markers. The data on sexual behaviour was self reported and therefore prone to recall bias and social desirability. Participants who did not attend all visits were less likely to have protected sex so this biased the results towards the null. Therefore the increase in protected sexual acts may have been higher than was found in our study due to

this selection bias from loss to follow up. Before and after studies are weak study designs compared to experimental studies because they lack randomisation and a comparison group.

Conclusion

This before and after study showed that counselling and provision of condoms to heterosexual HIV discordant couples as part of an HIV prevention trial may have contributed to increase in the rate of condom use and may therefore play an important role in the prevention of HIV. Both partners in an HIV discordant couple need to be involved in any HIV prevention strategies. HIV prevention trials involving HIV discordant couples are an important avenue for offering and piloting of specially designed counselling to these couples. In turn the same counselling can be useful in HIV testing and HIV management centres as a prevention strategy.

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PART D: APPENDICES

Appendix A: Supplementary results

Table V: Number of index participants who attended each visit

Visit (Month)	0	1	2	3	4	5	6	7	8	9	10	11	12
number	196	184	184	179	181	178	170	176	174	148	142	141	125

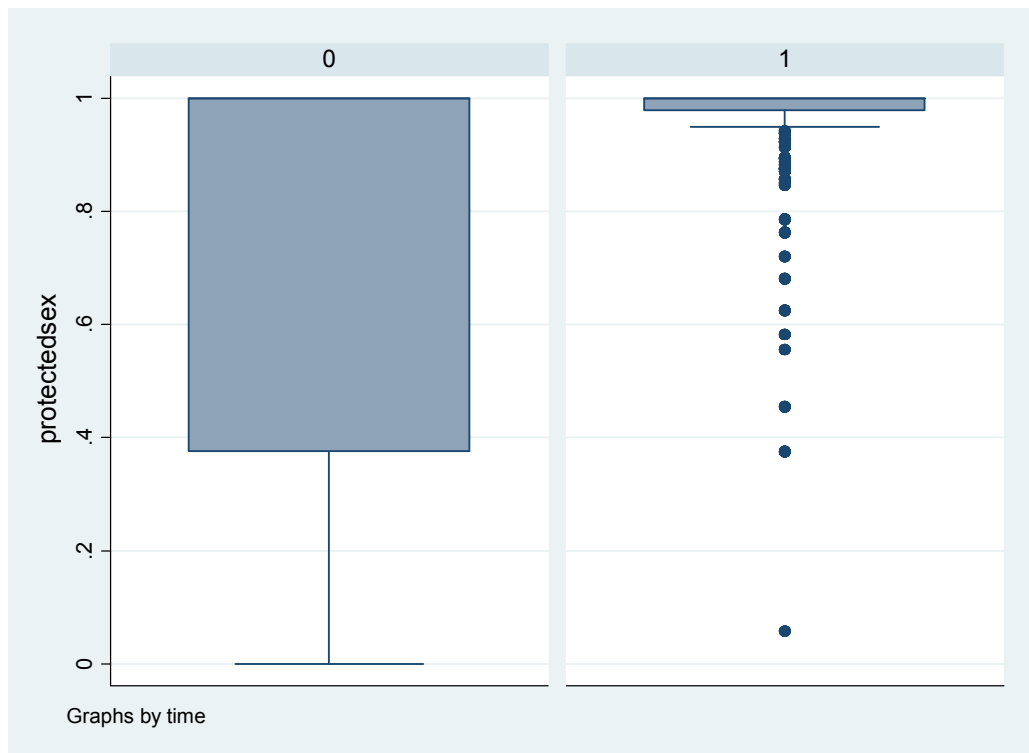
The number of index participants attending each visit reduced with time during the study.

Table VI: Number of index participants at each visit who reported at least one sexual act

Visit (month)	0	1	2	3	4	5	6	7	8	9	10	11	12
number	180	166	162	157	146	138	133	137	131	112	104	102	86

The number of index participants who reported at least one sexual act per visit decreased with time during the study.

Figure 7: Protected sex proportions at baseline and follow-up among all participants



0 (baseline)

1(follow-up)

The proportions of protected sex varied more at baseline than follow-up. During follow up there were very few couples having unprotected sex while most couples approached 100% condom use.

Table VII: Baseline and demographic characteristics of index heterosexual HIV discordant couples who completed follow up and those who were loss to follow up

	Index participants who completed study n=92		Index participants who did not complete study n=104	
Characteristic	Mean (Se)	C.I	Mean (Se)	C.I
Age	35.88 (0.99)	33.92 – 37.84	31.77 (0.86)	30.06 – 33.48
Years in school	8.76 (0.30)	8.17- 9.35	9.06 (0.24)	8.58 – 9.54
Characteristic	Frequency (%)	C.I ^a	Frequency (%)	C.I ^a
Females	72 (78)	0.68 – 0.86	82 (79)	0.70 – 0.86
Married to study partner	13 (14)	0.07 – 0.23	16 (15)	0.09 – 0.24
Living with study partner	64 (70)	0.59 – 0.79	55 (53)	0.43 – 0.63
Number earning an income	17 (18)	0.11 – 0.28	27 (26)	0.18 – 0.35
Resident in formal settlement	44 (48)	0.37- 0.58	54 (52)	0.42 – 0.62
<i>CI (Confidence interval) % (Percentage) Se (Standard error) n (number of participants)</i>				

^a binomial exact confidence interval

The index participants who did not complete the study were significantly younger than those who completed the study. It appeared as though more of those who completed the study lived with their study partner and more of those who did not complete the study earned an income but these were not statistically significant differences.

Table VIII: Baseline and demographic characteristics of partners of heterosexual HIV discordant couples who completed follow up and those who were lost to follow up

Partners whose index participants who completed study *n=92			Partners whose index participants who did not complete the study *n=104	
Characteristic	Mean (Se)	C.I	Mean (Se)	C.I
Age	38.05 (0.99)	33.92 –37.84	35.09 (0.86)	30.06 – 33.48
Years in school	8.34 (0.32)	7.70- 8.98	8.42 (0.25)	7.92 – 8.92
Characteristic	Frequency (%)	C.I ^a	Frequency (%)	C.I ^a
Females	20 (22)	0.14 – 0.32	22 (21)	0.14 – 0.30
Married to study partner	12 (13)	0.07 – 0.22	9 (18)	0.11 – 0.27
Living with study partner	68 (74)	0.64 – 0.82	58 (56)	0.46 – 0.66
Number earning an income	31 (34)	0.24 – 0.44	33 (32)	0.23 – 0.42
Resident in formal settlement	48 (52)	0.35 – 0.56	60 (58)	0.48 – 0.67
CI (Confidence interval) % (Percentage) Se (Standard error) n (number of participants)				

^a binomial exact confidence interval

The partners of index participants who completed the study were significantly older than partners of index participants who did not complete the study. It appeared as though more partners of index participants who completed the study lived with their study partner and more of those who did not complete the study lived in formal settlements but these were not statistically significant differences.

Table IX: Model selection summary of characteristics associated with use of condoms over one year of follow up.

	Model	Variable	AIC	p value ^a	Versus
1	A	Time(follow-up versus baseline)	2014.987	< 0.0001	N/A
2	B	Time, presence of other partners among index participant	2007.767	0.0024	Versus 1
3	V	Time, presence of other partners among index participant, earning by partner participant	2005.518	0.0393	Versus 2
4	X	Time, presence of other partners among index participant, earning by partner and earning by index participant	2004.442	0.0795	Versus 3
5	Z	Time, presence of other partners among index participant, earning by partner, earning by index participant, marriage	2005.916	0.4681	Versus 4

^a Likelihood ratio Chi-square test used to generate the p-value
Aikake's Information Criterion (AIC)

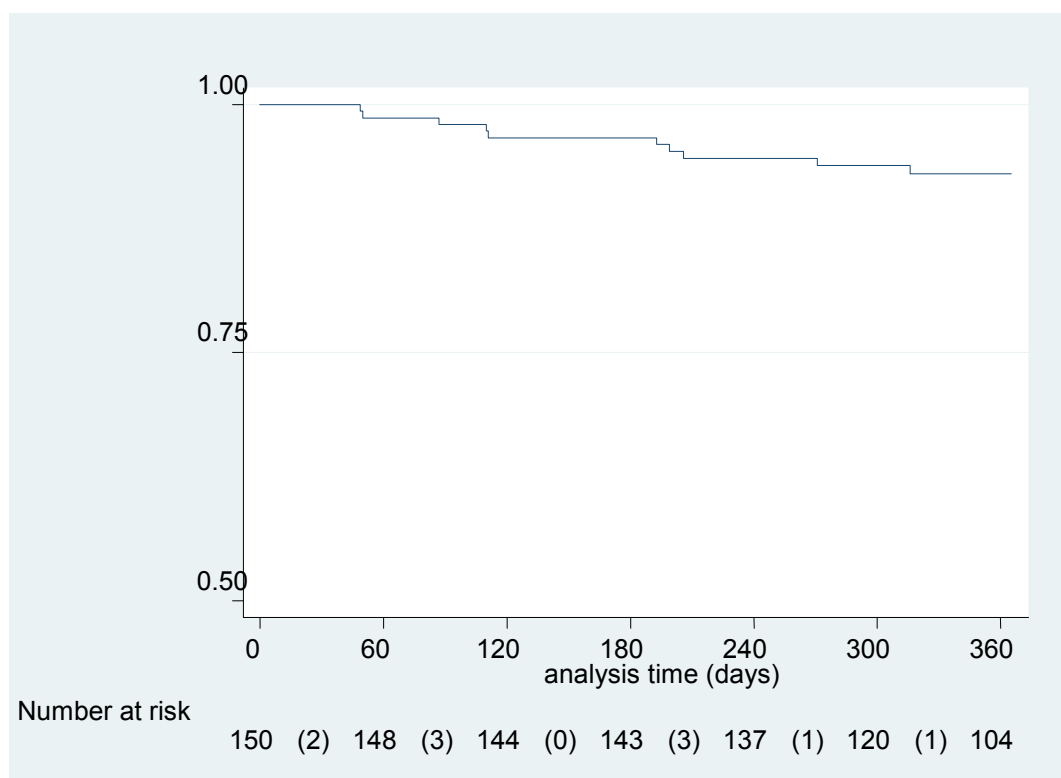
The best 1 variable model was model A with the time variable. It had the lowest AIC and was significantly better than the null model.

The best 2 variable model was B. It had the lowest AIC and was significantly better than model A. Presence of other partners contributed significantly to model A.

The best 3 variable model was V. It had the lowest AIC and was significantly better than model B. Earning by partner participant contributed significantly to model B.

The best 4 variable model was model X. It had the lowest AIC but was not significantly better than model X. Earning by index participant did not contribute significantly to model V.

Figure.8: Kaplan Meir survival estimates of time to pregnancy



The numbers in the bracket are the incident pregnancies at that point in time and the total outside the bracket is the number at risk at the same point in time.

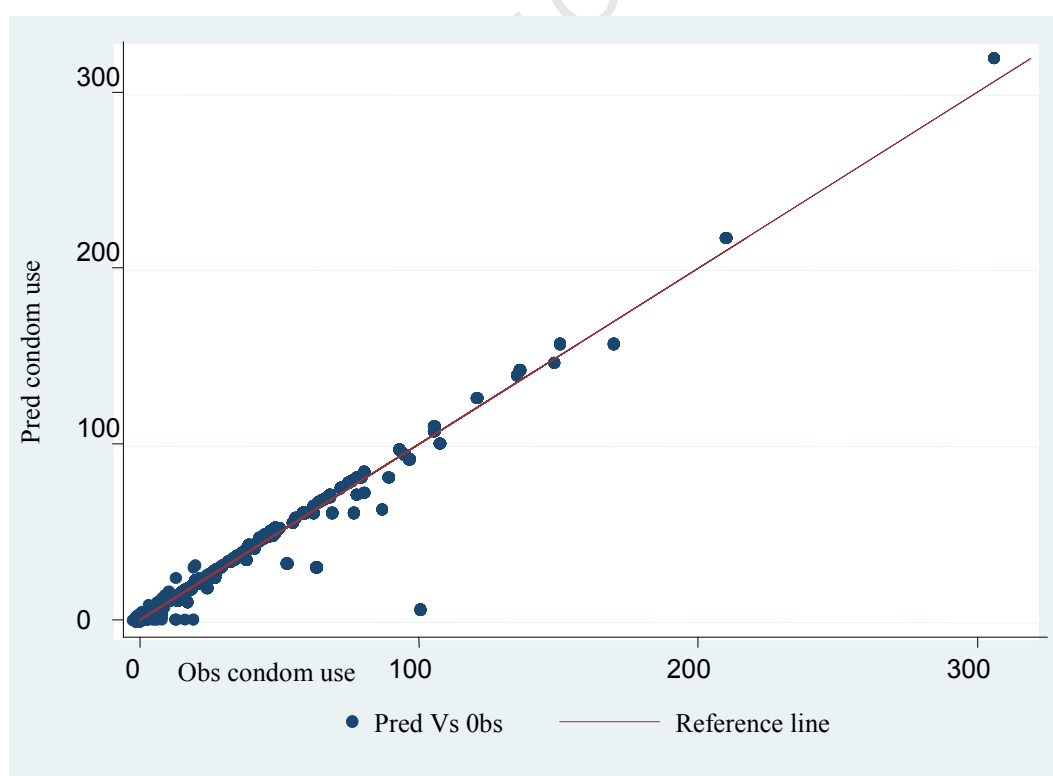
150 (2): means that in the first 60 days, 2 pregnancies occurred among the 150 females who were at risk.

Table X: Participants who were assessed for genital tract infection over the one year period.

Visit	Number of participants
3	179
6	170
9	148
12	125

The number of participants assessed for genital tract infections decreased over time

Figure 9: Predicted condom use from model against observed condom use reported by index participants



Pred – Predicted condom use by model

Obs – Observed condom use

The model had a good prediction of number of times condoms were used as showed by how close to the reference line the scatter points were.

University of Cape Town

Appendix B: Consent Form Index participants

Phase III Randomized Placebo-Controlled Trial of HSV-2 Suppression to Prevent HIV Transmission among HIV-Discordant Partners

ENROLLMENT FOR INDEX PARTICIPANTS

PRINCIPAL INVESTIGATOR: *[insert name]*

[insert physical address and other relevant contact info]

INFORMED CONSENT

We are asking you to volunteer for a research study. This study is for partners in whom one person has HIV and the other does not. HIV is the virus that causes AIDS. Before you decide whether to take part in the study, we would like to explain the purpose of the study, the risks and benefits, and what would be expected of you if you agree to be in the study. This study is sponsored by the Bill and Melinda Gates Foundation and the University of Washington, which are located in Seattle, Washington, USA.

PURPOSE OF THE STUDY

The research study will find out if a drug called acyclovir can help prevent passing HIV from a person who is HIV-infected and has genital herpes to their partner(s) during sex. Studies have shown that having genital herpes infection makes people with HIV more likely to pass HIV to others during sex. Genital herpes is caused by a virus called herpes simplex virus 2 or “HSV-2.” Like HIV, HSV-2 is passed from one person to another during sex. HSV-2 is a very common infection with as many as 2 out of 3 people infected in many parts Africa, India, and Latin America. Most people who have HSV-2 do not know they have it. In some people, HSV-2 causes sores or itching in the genital area. Some may not notice any symptoms. When HSV-2 is present in the genital area of someone who has HIV, the amount of HIV virus in their genital area increases. This is because the two viruses seem to interact in ways that increase the amount and frequency of both viruses in the genital area.

There is no cure for HSV-2, but an approved drug called acyclovir helps prevent and heal genital sores among people who have HSV-2. Acyclovir is not a treatment for HIV. But it is possible that, by treating HSV-2, acyclovir can help prevent passing HIV from one person to another.

Approximately 3000 couples, mostly from Africa, will be in the study. This will be the largest study of this kind ever, which may help us learn new ways to prevent HIV transmission. We will store blood for future studies of HIV, the immune system, and genes that may influence whether HIV is transmitted from one person to another.

200-400 couples are planned to be in the study here at [clinic]. We will ask you and your partner(s) to be in the study for up to 2 years. The whole study will take about 4 years to finish.

YOUR PARTICIPATION IS VOLUNTARY

This consent form gives information about the study that we will discuss with you. Once you understand the study, and if you agree to take part, we will ask you to sign your name or make your mark on this form. We will offer you a copy to keep.

Before you learn about the study procedures, it is important that you know the following:

- You do not have to be in this study if you do not want to join
- You may decide not to take part in the study, or to withdraw from the study at any time, without losing the benefits of your or your partner's routine medical care
- If you decide not to take part in the study, you can still join another research study later, if one is available and you qualify

STUDY GROUPS

If you and your partner are eligible and agree to take part in the study, we will randomly place you and your partner in 1 of 2 study groups. In one group, the partner with HIV will get acyclovir pills to take twice a day, every day. In the other group, the partner with HIV will get placebo pills to take twice a day, every day. The placebo pills look the same as the acyclovir pills, but do not contain acyclovir or any other medicine.

Your group will be chosen “by lot” [or other equivalent local term, for example, like flipping a coin or throwing dice]. You have an equal (or “50-50”) chance of being placed in each group. You and your partner cannot choose your group. The study staff also cannot choose your group. Neither you nor the study staff will know which group you are in. You cannot be told which group you are in until about 6-24 months after the end of the study. This means you may have to wait about 1½ to 4 years to find out whether you received acyclovir or placebo. After the study, if the study shows that suppressing herpes is effective in reducing the chances of passing HIV to your partner, you will be offered one year of free acyclovir as a benefit of being in the study.

Both groups are very important to this study. Couples in both groups will have the same study visits. All couples will get condoms, treatment for other STDs, and counseling on how to avoid HIV and other infections passed during sex.

No matter what study group you are in, you must remember that we do not know if acyclovir works to prevent passing HIV from one person to another. The only known way to prevent passing HIV during sex is to use a condom every time you have sex.

STUDY PROCEDURES

If you decide to take part in the study, your first visit will continue today, after you read, discuss, and sign or make your mark on this form.

You will be given a supply of acyclovir or placebo pills and instructions to take one pill twice a day, every day, for the next month.

You will receive a genital exam during this visit to look for STDs and to take samples for measuring HIV in genital secretions. You will also give blood [up to 57cc/3-4 tablespoons or local equivalent] that will be sent to study researchers at the University of Washington. The University of Washington researchers will confirm the results of the HIV and HSV-2 tests that we do here. Your blood will be tested for syphilis.

You and your partner will be in the study for up to 24 months (2 years). You will have study visits every month, for a total of at least 24 visits. Your partner will have study visits every 3 months, for a total of 8 visits. During the months when you and your partner both have a visit, you should come to the clinic together, for your convenience and so you can have counselling together as a couple. If it is not possible to come at the same time, you can come for your visits by yourself. Each visit will take about 60 minutes.

At each scheduled visit you will:

- Be asked questions about your health and your sexual practices.
- Return your bottle of study pills from the past month.
- Get a new bottle of study pills for the next month.
- Get condoms.
- Give urine for a pregnancy test (for women only).
- Get referrals for medical care and other services if you need them.
- Be asked for updated information on where you live and how to keep in contact with you.

The study staff will use this information to remind you of scheduled visits. If you miss a visit, the study staff will try to contact you by [site-specific methods]. They also may visit your home to find you. They will try to reach you through the contact people that you list. If they talk to these people, they will not tell them why they are trying to reach you.

Every 3 months you also will:

- Talk with study staff about ways to avoid passing HIV and other infections during sex. We encourage you to have this counselling with your partner, but you can have it by yourself if you wish.
- Have a genital exam. For both men and women, if any sores are seen during the exam, the study staff will swab the sore for testing later for HSV at the University of Washington. If the study staff think that the sore is herpes, they may give you acyclovir pills to take twice daily for 5 days, in addition to your regular study pills. If signs of other treatable STDs passed during sex are seen during this exam, the study staff will give you medicine to treat them as needed.
- Give blood approximately [21cc/< 2 tablespoons or local equivalent] from your arm that will be sent to the University of Washington for tests of the HIV in your blood, your immune system, and your genes.
- Only at the visit that is scheduled to take place three months after joining the study, men will be asked but not required to give a semen sample that will be sent to the University of Washington for tests of the HIV that may be in the semen. Men who choose not to give this sample may remain in the study.

Every 6 months you also will:

- Give some more blood [a total of 57.5ml/3-4 tablespoons or local equivalent] from your arm for a CD4 cell count test. This test gives information on how well your immune system is working, and whether you would benefit for treatment to prevent infections related to HIV infection or treatment for HIV.

If your partner becomes HIV infected:

- During the course of the study we will provide you with condoms and other materials to help prevent transmission of HIV to your partner. However it is possible that your partner can become HIV infected. If your partner becomes HIV infected, we will continue to provide counselling and other support. We will also collect other samples from both you and your partner to help us understand HIV transmission from one person to another. We will ask you to give blood [21 cc/<2 tablespoons or local equivalent].at these visits:
 - 2-4 weeks after your partner first tests positive for HIV
 - Then 3 months after your partner first tests positive for HIV

At your last visit, you also will:

- Give some more blood [a total of 57.5ml/3-4 tablespoons or local equivalent] for a syphilis test. The study staff will make arrangements with you to give you the results of these test results when they are available.

At any time in the study:

- If the study staff suspects that you may be pregnant, you will be asked to give urine for a pregnancy test.
- If you are having health problems that may be due to infections passed during sex, you will have a genital exam (as described above). If you have an infection passed during sex that is treatable you will receive medicine to treat the infection.
- You can have extra counselling and testing for HIV if needed between scheduled visits, either with your partner or by yourself.
- If you and your partner end your relationship before your last scheduled study visit, we will ask you to stay in the study as originally scheduled (for up to 2 years).

- If you decide to leave the study before your last scheduled study visit, we will ask you to have a final study visit with all the exams and tests listed above.

Specimen Storage and use of your samples for future studies:

We would like to save samples of your blood, urine, semen, and genital secretions at [local site] and at the University of Washington for future research by us and by other researchers. We will use these samples only for research related to how people get HIV, HSV, HIV-related diseases and sexually-transmitted infections. This will include testing for genes which may affect whether a person is more or less likely to get these infections. This research is experimental and these tests are not useful for your clinical care. Before your samples leave the clinic, they will be assigned a code and your name will not be on them. Your name will be linked to the code only at this clinic and only for five years after the study is completed. After that time, the link between your name and the code on your samples will be destroyed. An Institutional Review Board or Independent Ethics Committee, which watches over the safety and rights of research participants, must approve any future research studies using your samples. If you agree to store your samples, we will keep them for as long as there is sample that can be used for future research. If you do not want to have your samples saved for future research, you can still be in this study and your samples will be destroyed once testing for the study is completed. If you agree to store your samples now, but change your mind before the end of the study, let the study staff know and we will make sure that your samples do not get stored for future research. We will not sell your samples. Tests done on your samples may lead to a new invention or discovery. We have no plans to share any money or other benefits resulting from this invention or discovery with you.

RISKS AND/OR DISCOMFORTS

Acyclovir is a very safe and effective drug. It has been used to treat HSV-2 in about 40 million people. Side effects are rare. The most common side effects of acyclovir (seen in less than 1 of 10 people who take acyclovir) are nausea and headache and, less often, vomiting and diarrhoea. Kidney problems were not reported among more than 70,000 people who took acyclovir at the dose used in this study but have been occasionally seen in healthy elderly persons or in people with kidney disease who receive a higher dose than will be used in this study. This does not mean that kidney problems will never occur, but that they are very rare. Acyclovir is safe to take with other medications, except for probenecid, a medicine that sometimes is used to treat gout and syphilis. If you think that you may be taking probenecid at any time during this study, please tell the study staff.

You may feel discomfort or pain when your blood is drawn. You may feel dizzy or faint. You may have a bruise where the needle goes into your arm. You may feel discomfort during genital exams.

You may become embarrassed, worried, or anxious when talking about your sexual practices and ways to keep from passing HIV, HSV-2, and other infections to your partner. Talking about HIV and HSV-2 and finding out your partner's test results could cause problems between you and your partner. Trained counsellors will help you and your partner deal with any feelings or questions you may have.

The study staff will make every effort to protect your privacy and confidentiality while you are enrolled in the study. However, it is possible that others may learn that you are in the study. Because of this, they may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job, or being accepted by your family or community.

PREGNANCY

Acyclovir is not known to cause birth defects. No side effects in newborn babies have been reported, but we do not know for sure how safe acyclovir is for unborn babies. For this reason, women who become pregnant while in the study will be asked to stop taking the study pills.

BENEFITS

You may get no direct benefit from being in this study. **We do not know if acyclovir helps prevent passing HIV from one person to another.** Plus, you may not get the acyclovir pills. You may get the placebo pills. Study staff will remind you of the importance of using condoms to prevent passing HIV to your partner.

You or others may benefit in the future from information learned in this study. You also may get some personal satisfaction from being part of research on HIV. This is true no matter what study group you are in.

You will get counselling and testing for HIV. You will get free condoms. If you or your partner has health problems that may be due to infections passed during sex, you will get medicine to treat them, if needed. If you are in the study group that gets acyclovir, you may have fewer genital sores than you otherwise would. No matter what group you are in, if you have a genital sore that is caused by herpes, you may receive acyclovir to treat it. If the study shows that acyclovir reduces the chances of passing HIV to HIV uninfected partners, as a benefit of study participation, all participants will be offered daily acyclovir for an additional 12 months.

You will receive care and support related to your HIV infection while this study is ongoing. If your CD4 count drops to less than 200, you will be either referred to a clinic where you can receive antiretroviral medicines or offered antiretroviral drugs (ARVs) to treat your HIV infection. Depending on when you and your partner join the study, this care will be available to you and your partner, if needed, for a maximum of 2 years. This care will be either provided through a referral clinic or paid for by the study and will be provided [by the study staff or by the xxx organization; EACH SITE INSERT INFO ON WHAT IS AVAILABLE HERE]. After the study is over, the study staff will no longer be able to provide this care to you or your partner. You and your partner will be referred to other HIV care programs that are available to you (if any).

For other health problems, the study staff will give you care and treatment that is available at the clinic. [EACH SITE INSERT INFO ON WHAT IS AVAILABLE HERE]. For care and treatment that is not available at the clinic, study staff will tell you about other places where care and treatment may be available.

NEW FINDINGS

You will be told any new information learned during this study that is important for your health or might cause you to change your mind about staying in the study. You will be told when the results of the study may be available, and how to learn about them.

REASONS WHY YOU MAY BE WITHDRAWN FROM THE STUDY

You may be removed from the study without your consent for the following reasons:

- The study staff feels that staying in the study would be harmful to you.
- The study is stopped or cancelled.
- You are not able to attend study visits or complete the study procedures.

ALTERNATIVES TO PARTICIPATION

We do not know if acyclovir works to prevent passing HIV from one person to another during sex. The only known way to prevent passing HIV during sex is to use a condom every time you have sex.

[Sites to include/amend the following if applicable: There may be other studies going on here or in the community that you or your partner may be eligible for. If you wish, we will tell you about other studies that we know about. There also may be other places where you can go for HIV counselling and testing. We will tell you about those places if you wish.]

COSTS TO YOU

There is no cost to you for being in this study. Treatments available to you from the study will be given free of charge.

REIMBURSEMENT

[Sites to insert information about local incentives:]

You will receive money [*site specified amount*] for your time and effort at each scheduled study visit. You also will receive payment for the costs of [lost work, travel, and/or childcare] due to your visits.

CONFIDENTIALITY

Efforts will be made to keep your personal information confidential. However, absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law. Any sample from you or information about you will be identified only by code. The link between your name and code will be kept in a secure location at the clinic only. We will not discuss any information about you with your partner unless you give written permission, and will encourage you to be present during the discussion. Any publication of this study will not use your name or identify you personally.

Your study records may be reviewed by study staff and representatives of:

- the University of Washington, including study monitors
- the Bill and Melinda Gates Foundation
- [insert applicable local authorities, e.g., Ministry of Health]
- [insert names of applicable IRBs/ECs]

RESEARCH-RELATED INJURY

The study staff will monitor your health while you are in this study. You will have a study visit every month. If have any health problems between visits — especially nausea, vomiting, diarrhea, weight gain, or a decrease in the amount of urine you make — please contact the study staff. If you have a medical emergency that requires immediate care, [insert site-specific instructions].

[Sites to amend this sample text as needed, and/or specify institutional policy:] If you are injured as a result of being in the study, the study staff will give you immediate necessary treatment for your injuries, free of charge. The study staff also will tell you where you can get additional treatment for your injuries, if needed. There is no program for monetary compensation or other forms of compensation for such injuries.

PROBLEMS OR QUESTIONS

If you ever have any questions about this study, or if you have a research-related injury, you should contact [insert name of the investigator or other study staff] at [insert telephone number and/or physical address].

If you have questions about your rights as a research participant, you should contact [insert name or title of person on the IRB/EC or other organization appropriate for the site] at [insert telephone number and/or physical address of above].

STATEMENT OF CONSENT AND SIGNATURES

I have read this form or had it read to me. I have discussed the information with study staff. My questions have been answered. I understand that my decision whether or not to take part in the study is voluntary. I understand that if I decide to join the study I may withdraw at any time. By signing this form I do not give up any rights that I have as a research participant.

[Insert signature blocks as required by the local IRB/EC:]

_____	_____	_____
Participant Name	Participant Signature/Thumbprint	Date
(print)		
_____	_____	_____
Study Staff Conducting	Study Staff Signature	Date
Consent Discussion (print)		
_____	_____	_____
Witness Name	Witness Signature	Date
(print)		

CONTINUED FOLLOW-UP:

Please initial and date one option:

_____ I DO agree to continued follow-up of up to 2 years (24 months)

_____ I DO NOT agree to continued follow-up of up to 2 years (24 months)

_____	_____	_____
Witness Name	Witness Signature	Date
(print)		

SPECIMEN STORAGE AND USE OF YOUR SAMPLES FOR FUTURE STUDIES:

Please initial and date one option:

_____ I DO agree to store my samples for future research

_____ I DO NOT agree to store my samples for future research

_____	_____	_____
Witness Name	Witness Signature	Date
(print)		

Appendix C: Consent Form Partner participants

Phase III Randomized Placebo-Controlled Trial of HSV-2 Suppression to Prevent HIV Transmission among HIV-Discordant Couples

ENROLLMENT FOR PARTNER PARTICIPANTS

PRINCIPAL INVESTIGATOR: *[insert name]*

[insert physical address and other relevant contact info]

INFORMED CONSENT

We are asking you to volunteer for a research study. This study is for partners in whom one person has HIV and the other does not. HIV is the virus that causes AIDS. Before you decide whether to take part in the study, we would like to explain the purpose of the study, the risks and benefits, and what would be expected of you if you agree to be in the study. This study is sponsored by the Bill and Melinda Gates Foundation and the University of Washington, which are located in Seattle, Washington, USA.

PURPOSE OF THE STUDY

The research study will find out if a drug called acyclovir can help prevent passing HIV from a person who is HIV-infected and has genital herpes to their partner(s) during sex. Studies have shown that having genital herpes infection makes people with HIV more likely to pass HIV to others during sex. Genital herpes is caused by a virus called herpes simplex virus 2 or “HSV-2.” Like HIV, HSV-2 is passed from one person to another during sex. HSV-2 is a

very common infection with as many as 2 out of 3 people infected in many parts Africa, India, and Latin America. Most people who have HSV-2 do not know they have it. In some people, HSV-2 causes sores or itching in the genital area. Some may not notice any symptoms. When HSV-2 is present in the genital area of an HIV-infected person, the amount of HIV virus in the genital area increases. This is because the two viruses seem to interact in ways that increase the amount and frequency of both viruses in the genital area.

There is no cure for HSV-2, but an approved drug called acyclovir helps prevent and heal genital sores among people who have HSV-2. Acyclovir is not a treatment for HIV. But it is possible that, by treating HSV-2, acyclovir can help prevent passing HIV from one person to another.

Approximately 3000 couples, mostly from Africa, will be in the study. This will be the largest study of this kind ever, which may help us learn new ways to prevent HIV transmission. We will store blood for future studies of HIV, the immune system, and genes that may influence whether HIV is transmitted from one person to another.

200-400 couples are planned to be in the study here at [clinic]. We will ask you and your partner(s) to be in the study for up to 2 years. The whole study will take about 4 years to finish.

YOUR PARTICIPATION IS VOLUNTARY

This consent form gives information about the study that we will discuss with you. Once you understand the study, and if you agree to take part, we will ask you to sign your name or make your mark on this form. We will offer you a copy to keep.

Before you learn about the study procedures, it is important that you know the following:

- You do not have to be in this study if you do not want to join
- You may decide not to take part in the study, or to withdraw from the study at any time, without losing the benefits of your or your partner's routine medical care
- If you decide not to take part in the study, you can still join another research study later, if one is available and you qualify

STUDY GROUPS

If you and your partner are eligible and agree to take part in the study, we will randomly place you and your partner in 1 of 2 study groups. In one group, the partner with HIV will get acyclovir pills to take twice a day, every day. In the other group, the partner with HIV will get placebo pills to take twice a day, every day. The placebo pills look the same as the acyclovir pills, but do not contain acyclovir or any other medicine.

Your group will be chosen "by lot" [or other equivalent local term, for example, like flipping a coin or throwing dice]. You have an equal (or "50-50") chance of being placed in each group. You and your partner cannot choose your group. The study staff also cannot choose your group. Neither you nor the study staff will know which group you are in. You cannot be told which group you are in until about 6-24 months after the end of the study. This means you may have to wait up from about 1 ½ to 4 years to find out.

Both groups are very important to this study. Couples in both groups will have the same study visits. All couples will get condoms, treatment for other STDs, and counseling on how to avoid HIV and other infections passed during sex.

No matter what study group you are in, you must remember that we do not know if acyclovir works to prevent passing HIV from one person to another. The only known way to protect against getting HIV during sex is to use a condom every time you have sex.

STUDY PROCEDURES

If you decide to take part in the study, your first visit will continue today, after you read, discuss, and sign or make your mark on this form.

You will receive a genital exam to look for STDs. You will give blood [up to 57.5cc/3-4 tablespoons or local equivalent] today that will be sent to study researchers at the University of Washington. These researchers will confirm the results of the HIV and HSV-2 tests that we do here and will look for other genetic, infectious and immune factors that affect the chances of becoming HIV-infected. You will be offered counselling about your HSV-2 blood test results. Your blood will be tested for syphilis and HSV-2.

You and your partner will be in the study for up to 24 months (2 years). During the months when you and your partner both have a visit, you should come to the clinic together, for your convenience and so you can have counselling together as a couple. If that is not possible, you can come for your visits by yourself if you wish. Each visit will take about 60 minutes.

At each scheduled visit you will:

- Be asked questions about your health and your sexual practices.
- Have a genital exam. If any sores are seen during this exam the study staff will swab the sore for later testing for HSV-2 at the University of Washington. If the study staff think that the sore is herpes, they may give you acyclovir pills to take twice daily for 5 days. If signs of other bacterial infections passed during sex are seen during this exam, the study staff will give you medicine to treat them as needed.
- Talk with study staff about ways to avoid HIV and other infections passed during sex. We encourage you to have this counselling with your partner, but you can have it by yourself if you wish.
- Talk with study staff about the HIV test and give blood [21 cc/2 tablespoons or local equivalent] from your arm for the test. When we do HIV testing for this study, we first do a test that gives results in about 20 minutes. You will get the result of that test when it is available on the same day you give blood and have the test. If the test shows that you may have HIV infection, we will do another different test to confirm this result. This test takes about 1-2 weeks, so you will have to come back here at that time to get the results. You will talk with the study staff about the meaning of your results and how you feel about them. Sometimes HIV tests are not clearly positive but also not negative. In that case, we will do more tests until we know the result for sure. You must receive your HIV test results to stay in the study.
- Get condoms.
- Get referrals for medical care and other services if you need them.

- Give updated information on where you live and how to keep in contact with you. The study staff will use this information to remind you of scheduled visits. If you miss a visit, the study staff will try to contact you by [site-specific methods]. They also may visit your home to find you. They will try to reach you through the contact people that you list. If they talk to these people, they will not tell them why they are trying to reach you.

Every 3 months, you also will:

- Give some more blood [up to 57.5 cc/3-4 tablespoons or local equivalent] for an HIV test and to send to study researchers at the University of Washington to look for genetics, infectious and immune factors that affect the chances of becoming HIV-infected.

If you become HIV infected:

- During the course of the study we will provide you with condoms and other materials to help prevent transmission of HIV to your partner. However it is possible that you can become HIV infected. If you become HIV infected, we will continue to provide counselling and other support.

- If your HIV test result shows that you are infected with HIV, the study staff will talk with you about this test result and what this means for you. The staff will obtain a second blood test to confirm the initial positive test and you will be referred for care and additional counselling and services available to you. If you do become infected with HIV, we will ask that you continue your scheduled study visits every 3 months. We will collect other samples from both you and your partner to help us understand HIV transmission from one person to another. We will ask you to give blood [57.5 cc/3-4 tablespoons or local equivalent].at these visits:
 - When you first test positive for HIV
 - 2-4 weeks after you first tests positive for HIV
 - Then every 3 months (quarterly) after your first positive test for HIV. This follow-up will continue for a total of 12 months after your first positive test for HIV.

At your last visit, you also will:

- Give some more blood [up to 57.5 cc/3-4 tablespoons or local equivalent] for tests for syphilis. The study staff will make arrangements with you to give you the results of these test results when they are available.

At any time in the study:

- If you or the study staff thinks you may be pregnant, you will give urine for a pregnancy test (for women only).
- If you are having health problems that may be due to bacterial infections passed during sex, you will have a genital exam (as described above) and receive medicine to treat the infections as needed.
- You can have extra counselling and testing for HIV if needed between scheduled visits, either with your partner or by yourself.

- If you and your partner end your relationship before your last scheduled study visit, we will ask you to stay in the study as originally scheduled (for 2 years).
- If you decide to leave the study before your last scheduled study visit, we will ask you to have a final study visit with all the exams and tests listed above.

Specimen Storage and use of your samples for future studies:

We would like to save samples of your blood, urine, semen, and genital secretions at [local site] and at the University of Washington for future research by us and by other researchers. We will use these samples only for research related to how people get HIV, HSV, HIV-related diseases and sexually-transmitted infections. This will include testing for genes which may affect whether a person is more or less likely to get these infections. This research is experimental and these tests are not useful for your clinical care. Before your samples leave the clinic, they will be assigned a code and your name will not be on them. Your name will be linked to the code only at this clinic and only for five years after the study is completed. After that time, the link between your name and the code on your samples will be destroyed. An Institutional Review Board or Independent Ethics Committee, which watches over the safety and rights of research participants, must approve any future research studies using your samples. If you agree to store your samples, we will keep them for as long as there is sample that can be used for future research. If you do not want to have your samples saved for future research, you can still be in this study and your samples will be destroyed once testing for this study is completed. If you agree to store your samples now, but change your mind before the end of the study, let the study staff know and we will make sure that your samples do not get stored for future research. We will not sell your samples. Tests done on your samples may lead to a new invention or discovery. We have no plans to share any money or other benefits resulting from this invention or discovery with you.

RISKS AND/OR DISCOMFORTS

You may feel discomfort or pain when your blood is drawn. You may feel dizzy or faint. You may have a bruise where the needle goes into your arm. You may feel discomfort during genital exams.

You may become embarrassed, worried, or anxious when talking about your sexual practices, ways to protect against HIV and other infections passed during sex, and your HIV and HSV-2 test results. You may become worried or anxious while waiting for your test results. If you have or become infected with HIV or HSV-2, knowing this could make you worried or anxious. Talking about HIV and HSV-2 and finding out your test results could cause problems between you and your partner. Trained counsellors will help you and your partner deal with any feelings or questions you may have.

The study staff will make every effort to protect your privacy and confidentiality while you are having the study procedures. However, it is possible that others may learn of your participation here and, because of this, may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job, or being accepted by your family or community.

BENEFITS

You may get no direct benefit from being in this study. **We do not know if acyclovir helps prevent passing HIV from one person to another.** Plus, your partner may not get the acyclovir pills. He/she may get the placebo pills. Study staff will remind you of the importance of using condoms to protect against HIV.

You or others may benefit in the future from information learned in this study. You also may get some personal satisfaction from being part of research on HIV. This is true no matter what study group you are in.

You will get counselling and testing for HIV. You will get free condoms. If you or your partner has health problems that may be due to infections passed during sex, you will get medicine to treat them, if needed. If you have a genital sore that is caused by herpes, you may receive acyclovir to treat it. For other health problems, the study staff will give you care and treatment that is available at the clinic. [EACH SITE INSERT INFO ON WHAT IS AVAILABLE HERE]. For care and treatment that is not available at the clinic, study staff will tell you about other places where care and treatment may be available.

Your partner will receive care and support related to his/her HIV infection while this study is ongoing. Depending on when you and your partner join the study, this care will be available to your partner for a maximum of 2 years. This care will be either be provided through a referral clinic or paid for by the study and will be provided [by the study staff or by the xxx organization]. Medications used to treat HIV will be given per guidelines of the World Health Organization for at least two years. If you become infected with HIV while in this study, you will be offered counselling and clinical services for HIV while the study is ongoing. After the study is over, the study staff will no longer be able to provide this care to you or your partner. You and your partner will be referred to other HIV care programs that are available to you (if any).

NEW FINDINGS

You will be told any new information learned during this study that is important for your health or might cause you to change your mind about staying in the study. You will be told when the results of the study may be available, and how to learn about them.

REASONS WHY YOU MAY BE WITHDRAWN FROM THE STUDY

You may be removed from the study without your consent for the following reasons:

1. The study is stopped or cancelled.
2. The study staff feel that staying in the study would be harmful to you.
3. You are not able to attend study visits or complete the study procedures.

ALTERNATIVES TO PARTICIPATION

We do not know if acyclovir works to prevent passing HIV from one person to another during sex. The only known way to protect against HIV during sex is to use a condom every time you have sex.

[Sites to include/amend the following if applicable: There may be other studies going on here or in the community that you or your partner may be eligible for. If you wish, we will tell you about other studies that we know about. There also may be other places where you can go for HIV counselling and testing. We will tell you about those places if you wish.]

COSTS TO YOU

There is no cost to you for being in this study. Treatments available to you from the study will be given free of charge.

REIMBURSEMENT

[Sites to insert information about local incentives:]

You will receive money for your transportation costs, time and effort at each scheduled study visit. You also will receive payment for the costs of [lost work, travel, and/or childcare] due to your visits.

CONFIDENTIALITY

Efforts will be made to keep your personal information confidential. However absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law. Any sample from you or information about you will be identified only by code. The link between your name and code will be kept in a secure location at the clinic only. We will not discuss any information about you with your partner unless you give written permission, and will encourage you to be present during the discussion. Any publication of this study will not use your name or identify you personally.

Your study records may be reviewed by study staff and representatives of:

- the University of Washington, including study monitors
- the Bill and Melinda Gates Foundation
- [insert applicable local authorities, e.g., Ministry of Health]
- [insert names of applicable IRBs/ECs]

RESEARCH-RELATED INJURY

The study staff will monitor your health and the health of your partner while you are in this study. You will have a study visit every 3 months. Your partner will have a visit every month. If you or your partner has any health problems between visits, please contact the study staff. If you have a medical emergency that requires immediate care, [insert site-specific instructions].

[Sites to amend this sample text as needed, and/or specify institutional policy:] If you are injured as a result of being in the study, the study staff will give you immediate necessary treatment for your injuries, free of charge. The study staff also will tell you where you can get additional treatment for your injuries, if needed. There is no program for monetary compensation or other forms of compensation for such injuries.

PROBLEMS OR QUESTIONS

If you ever have any questions about this study, or if you have a research-related injury, you should contact [insert name of the investigator or other study staff] at [insert telephone number and/or physical address].

If you have questions about your rights as a research participant, you should contact [insert name or title of person on the IRB/EC or other organization appropriate for the site] at [insert telephone number and/or physical address of above].

STATEMENT OF CONSENT AND SIGNATURES

I have read this form or had it read to me. I have discussed the information with study staff. My questions have been answered. I understand that my decision whether or not to take part in the study is voluntary. I understand that if I decide to join the study I may withdraw at any time. By signing this form I do not give up any rights that I have as a research participant.

[Insert signature blocks as required by the local IRB/EC:]

Participant Name

(print)

Participant Signature/Thumbprint

Date

Study Staff Conducting

Consent Discussion (print)

Study Staff Signature

Date

Witness Name

(print)

Witness Signature

Date

CONTINUED FOLLOW-UP:

Please initial and date one option:

_____ I DO agree to continued follow-up of up to 2 years (24 months)

_____ I DO NOT agree to continued follow-up of up to 2 years (24 months)

_____	_____	_____
Witness Name	Witness Signature	Date
(print)		

SPECIMEN STORAGE AND USE OF YOUR SAMPLES FOR FUTURE STUDIES:

Please initial and date one option:

_____ I DO agree to store my samples for future research

_____ I DO NOT agree to store my samples for future research

_____	_____	_____
Witness Name	Witness Signature	Date
(print)		

Appendix D: Questionnaires

Partners in Prevention Study

Index Enrollment Sexual Risk Behavior (IESX)

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020

(IESX) 100

Visit Code 00.0

Participant ID: - - <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Form Completion Date: <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>
Index Enrollment Sexual Risk Behavior <i>This is an interviewer-administered form. Read each item aloud to the participant.</i>	
<p>Now I'm going to ask you about your sexual practices. While some of this information may be embarrassing or difficult to remember, please try to give your best answers and be as honest as you can. Whenever "sex" or "sexual intercourse" is stated, it includes vaginal and anal sex, but not oral sex. The term "condom" refers to either a male or female condom.</p> <p>Now we will ask you about your study partner(s). (If more than one partner, items 1 and 2 refer to partner participant #1; item 3 refers to sexual partners not participating in the study.)</p>	
1	<p>In the past month, how many times did you have sexual intercourse with your study partner?</p> <div style="display: flex; align-items: center;"> number of sex acts </div> <p style="text-align: right; margin-top: -10px;">→ If 0, go to item 2.</p> <p>1a. Of those times, how often was a condom used?</p> <div style="display: flex; align-items: center;"> number of times condom used </div>
2	<p>When having sex, do you and your study partner ever use anything to reduce the secretions or make the vagina dry?</p> <div style="display: flex; justify-content: space-between;"> <input type="checkbox"/> yes <input type="checkbox"/> no </div> <p style="text-align: right; margin-top: -10px;">→ If no, go to item 3.</p> <p>2a. What have you used to make the vagina dry?</p> <p>_____</p> <p>2b. How often do you use something to make the vagina dry?</p> <div style="display: flex; justify-content: space-around;"> <input type="checkbox"/> rarely <input type="checkbox"/> sometimes <input type="checkbox"/> most of the time <input type="checkbox"/> always </div>
3	<p>Besides the study partner(s), how many partners have you had sex with in the past month?</p> <div style="display: flex; align-items: center;"> number of partners </div> <p style="text-align: right; margin-top: -10px;">→ If 0, go to item 4.</p> <p>3a. How many of these are new partners?</p> <div style="display: flex; align-items: center;"> number of new partners </div> <p>3b. In the past month, how many times did you have sexual intercourse with someone other than your study partner(s)?</p> <div style="display: flex; align-items: center;"> number of sex acts </div> <p style="text-align: right; margin-top: -10px;">→ If 0, go to item 4.</p> <p>3b1. Of those times, how often was a condom used?</p> <div style="display: flex; align-items: center;"> number of times condom used </div>
<p>Item 4 is for females only.</p>	
4	<p>Are you currently using birth control? <i>Mark only the primary method.</i></p> <div style="display: flex; flex-wrap: wrap;"> <div style="width: 33%;"><input type="checkbox"/> no/none</div> <div style="width: 33%;"><input type="checkbox"/> injectable</div> <div style="width: 33%;"><input type="checkbox"/> tubal ligation/hysterectomy</div> <div style="width: 33%;"><input type="checkbox"/> oral</div> <div style="width: 33%;"><input type="checkbox"/> implants</div> <div style="width: 33%;"><input type="checkbox"/> other, specify: _____</div> <div style="width: 33%;"><input type="checkbox"/> IUD</div> <div style="width: 33%;"><input type="checkbox"/> condoms only</div> </div>
<div style="display: flex; justify-content: space-between;"> Version 1.0, 27-10-04 English Completed by: _____ (initials/date) </div>	

SAMPLE: DO NOT FAX TO DATAFAX

(Partners) 020

(IESX) 100

Visit Code 00.00

Participant ID: - - - <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Form Completion Date: <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>									
Index Enrollment Sexual Risk Behavior <i>This is an interviewer-administered form. Read each item aloud to the participant.</i>										
<p>Ngoku ndizakubuzwa ngezesondo. Nangona olu lwazi lusenkubanga iintloni okanye kubenzima ukukhumbula, nceda uzame kangangoko unakho ukunika impendulo enyanisekileyo. Nanini na kuthethwa ngesondo okanye ukwabelana ngesondo, kubandakanya ukwabelana ngesondo ebufazini nangasemva kodwa hayi emlonyeni. Igama elithi khondom libhekiselele kwikhondom yabafazi okanye eyamadoda.</p> <p>Ngoku sizakubuzwa ngeqabane okanye amaqabane akho ophando. (If more than one study partner, items 1 and 2 refer to partner participant #1; item 3 refers to sexual partners not participating in the study.)</p>										
1	<p>Kule nyanga iphelileyo, wabelane kangaphi ngesondo neqabane lakho elikuphando? inani lezihlandlo zokwabelana ngesondo If 0, go to item 2.</p> <p>1a. Kulawo maxesha, sisetyenziswe kangaphi isingxobo sokuzikhusela? amaxesha ekusetyenziswe ngawo izingxobo zokuzikhusela</p>									
2	<p>Xa nisabelana ngesondo, wena neqabane lakho lophando nakhe nasebenzisa nto na ngamanye amaxesha ukunciphisa incindi okanye ukomisa ubufazi? <input type="checkbox"/> ewe <input type="checkbox"/> hayi If no, go to item 3.</p> <p>2a. Benikhe nasebenzisa ntoni ukomisa ubufazi? _____</p> <p>2b. Kuxhaphake kangakanani ukusebenzisa into yokomisa ubufazi bakho? <input type="checkbox"/> kunqabile <input type="checkbox"/> ngamanye amaxesha <input type="checkbox"/> amaxesha amaninzi <input type="checkbox"/> ngalo lonke ixesha</p>									
3	<p>Ngaphandle kweqabane lakho elikuphando, mangaphi amanye amaqabane okhe wabelana nawo ngesondo kulenyanga iphelileyo? inani lamaqabane If 0, go to item 4.</p> <p>3a. Kulamaqabane mangaphi amaqabane amatsha? inani lamaqabane amatsha</p> <p>3b. Kulenyanga iphelileyo, wabelane kangaphi ngesondo nomnye umntu ngaphandle kweqabane / (amaqabane) lakho elikuphando? inani lezihlandlo zokwabelana ngesondo If 0, go to item 4.</p> <p>3b1. Kulawo maxesha, sisetyenziswe kangaphi isingxobo sokuzikhusela? amaxesha ekusetyenziswe ngawo izingxobo zokuzikhusela</p>									
Item 4 is for females only.										
4	<p>Ungaba usebenzisa ucwangciso ntsapho? <i>Mark only the primary method.</i></p> <table style="width: 100%; border: none;"> <tr> <td><input type="checkbox"/> hayi okanye azikho</td> <td><input type="checkbox"/> ehlatywayo</td> <td><input type="checkbox"/> Ukuvala ukungazali okanye ukukhutshwa kwesibebeke</td> </tr> <tr> <td><input type="checkbox"/> okomlomo</td> <td><input type="checkbox"/> ezifakelweyo</td> <td><input type="checkbox"/> ezinye: _____</td> </tr> <tr> <td><input type="checkbox"/> isithinteli nzala esifakwa ngaphakathi esibebekeweni (luphu)</td> <td><input type="checkbox"/> khondom</td> <td></td> </tr> </table>	<input type="checkbox"/> hayi okanye azikho	<input type="checkbox"/> ehlatywayo	<input type="checkbox"/> Ukuvala ukungazali okanye ukukhutshwa kwesibebeke	<input type="checkbox"/> okomlomo	<input type="checkbox"/> ezifakelweyo	<input type="checkbox"/> ezinye: _____	<input type="checkbox"/> isithinteli nzala esifakwa ngaphakathi esibebekeweni (luphu)	<input type="checkbox"/> khondom	
<input type="checkbox"/> hayi okanye azikho	<input type="checkbox"/> ehlatywayo	<input type="checkbox"/> Ukuvala ukungazali okanye ukukhutshwa kwesibebeke								
<input type="checkbox"/> okomlomo	<input type="checkbox"/> ezifakelweyo	<input type="checkbox"/> ezinye: _____								
<input type="checkbox"/> isithinteli nzala esifakwa ngaphakathi esibebekeweni (luphu)	<input type="checkbox"/> khondom									
<div style="display: flex; justify-content: space-between;"> Version 1.0, 03-02-05 Xhosa Completed by: _____ (initials/date) </div>										

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020

(IFSX-1) 200

Visit Code .

Participant ID: <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Visit Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>
Index Follow-up Sexual Risk Behavior, page 1 <i>This is an interviewer-administered form. Read each item aloud to the participant.</i>	
<p>Now I'm going to ask you about your sexual practices. While some of this information may be embarrassing or difficult to remember, please try to give your best answers and be as honest as you can. Whenever "sex" or "sexual intercourse" is stated, it includes vaginal and anal sex, but not oral sex. The term "condom" refers to either a male or female condom.</p>	
1 Since the last regularly scheduled visit, how many times did you have sexual intercourse with your study partner? <i>(If more than one partner, these questions refer to partner participant #1.)</i> 1a. Of those times, how often was a condom used?	<div style="display: flex; align-items: center;"> <input type="text"/> <input type="text"/> <input type="text"/> number of sex acts </div> <div style="text-align: right; margin-top: -10px;">→ If 0, go to item 2.</div> <div style="display: flex; align-items: center; margin-top: 10px;"> <input type="text"/> <input type="text"/> <input type="text"/> number of times condom used </div>
1b. How long has it been since you last had sex with your study partner?	<div style="display: flex; align-items: center;"> <input type="text"/> <input type="text"/> <div style="margin-left: 10px;"> <input type="checkbox"/> days <input type="checkbox"/> weeks <input type="checkbox"/> months </div> </div>
1c. During this most recent encounter, was a condom used?	<div style="display: flex; align-items: center;"> <input type="checkbox"/> yes <input style="margin-left: 20px;" type="checkbox"/> no </div>
2 Besides the study partner(s), how many partners have you had sex with in the past month? 2a. How many of these are new partners? 2b. In the past month, how many times did you have sexual intercourse with someone other than your study partner(s)? 2b1. Of those times, how often was a condom used?	<div style="display: flex; align-items: center;"> <input type="text"/> <input type="text"/> <input type="text"/> number of partners </div> <div style="text-align: right; margin-top: -10px;">→ If 0, go to item 3.</div> <div style="display: flex; align-items: center; margin-top: 10px;"> <input type="text"/> <input type="text"/> <input type="text"/> number of new partners </div> <div style="display: flex; align-items: center; margin-top: 10px;"> <input type="text"/> <input type="text"/> <input type="text"/> number of sex acts </div> <div style="text-align: right; margin-top: -10px;">→ If 0, go to item 3.</div> <div style="display: flex; align-items: center; margin-top: 10px;"> <input type="text"/> <input type="text"/> <input type="text"/> number of times condom used </div>
Item 3 is for females only. Males continue to item 4.	
3 Are you currently using birth control? <i>Mark only the primary method.</i> <input type="checkbox"/> no/none <input type="checkbox"/> injectable <input type="checkbox"/> tubal ligation/hysterectomy <input type="checkbox"/> oral <input type="checkbox"/> implants <input type="checkbox"/> other, specify: _____ <input type="checkbox"/> IUD <input type="checkbox"/> condoms only	
Item 4 is not interviewer-administered.	
4 How many partners are enrolled for this index participant?	<div style="display: flex; align-items: center;"> <input type="text"/> number of partners </div> <div style="text-align: right; margin-top: -10px;">→ If only one partner, stop. If more than one enrolled partner, complete page 2 of the Index Follow-up Sexual Risk Behavior form (IFSX-2).</div>
Version 1.0, 27-10-04 English Completed by: _____ (initials/date)	

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020

(IFSX-2) 210

Visit Code

Participant ID: <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> - <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Form Completion Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>
Index Follow-up Sexual Risk Behavior, page 2 <i>This is an interviewer-administered form. Read each item aloud to the participant.</i>	
<i>If only one partner participant enrolled with this index participant, do not complete this page of the form. Sexual behavior with additional partner participants is recorded here.</i>	
5 Partner #2 ID	<input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> - <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: x-small;"> Site Couple I/P Chk </div>
6 Since the last regularly scheduled visit, how many times did you have sexual intercourse with your study partner?	<input type="text"/> <input type="text"/> <input type="text"/> number of sex acts If 0, go to item 7.
6a. Of those times, how often was a condom used?	<input type="text"/> <input type="text"/> <input type="text"/> number of times condom used
6b. How long has it been since you last had sex with your study partner?	<input type="text"/> <input type="text"/> <input type="checkbox"/> days <input type="checkbox"/> weeks <input type="checkbox"/> months
6c. During this most recent encounter, was a condom used?	<input type="checkbox"/> yes <input type="checkbox"/> no
7 Partner #3 ID	<input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> - <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: x-small;"> Site Couple I/P Chk </div>
8 Since the last regularly scheduled visit, how many times did you have sexual intercourse with your study partner?	<input type="text"/> <input type="text"/> <input type="text"/> number of sex acts If 0, end of form.
8a. Of those times, how often was a condom used?	<input type="text"/> <input type="text"/> <input type="text"/> number of times condom used
8b. How long has it been since you last had sex with your study partner?	<input type="text"/> <input type="text"/> <input type="checkbox"/> days <input type="checkbox"/> weeks <input type="checkbox"/> months
8c. During this most recent encounter, was a condom used?	<input type="checkbox"/> yes <input type="checkbox"/> no
Version 1.0, 27-10-04	English
Completed by: _____ (initials/date)	

SAMPLE: DO NOT FAX TO DATAFAX

(Partners) 020

(IFSX-1) 200

Visit Code

Participant ID: <input type="text"/> - <input type="text"/> - <input type="text"/> - <input type="text"/>	Visit Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
Site Couple I/P Chk	dd mm yy

Index Follow-up Sexual Risk Behavior, page 1 This is an interviewer-administered form. Read each item aloud to the participant.

Ngoku ndizakukubuza ngezesondo. Nangona olu lwazi lusenkubanga iintloni okanye kubenzima ukukhumbula, nceda uzame kangangoko unakho ukunika impendulo enyanisekileyo. Nanini na kuthethwa ngesondo okanye ukwabelana ngesondo, kubandakanya ukwabelana ngesondo ebufazini nangasemva kodwa hayi emlonyeni. Igama elithi khondom libhekiselele kwikhondom yabafazi okanye eyamadoda.

1	Ukusukela kutyalelo lwakho lokugqibela lwarhoqo, wabelane kangaphi ngesondo neqabane lakho elikuphando? (If more than one study partner, these questions refer to partner participant #1.)	<input type="text"/> <input type="text"/> <input type="text"/>	inani lezihlundo zokwabelana ngesondo → If 0, go to item 2.
1a.	Kulawo maxesha, sisetyenziswe kangaphi isingxobo sokuzikhusela?	<input type="text"/> <input type="text"/> <input type="text"/>	amaxesha ekusetyenziswe ngawo izingxobo zokuzikhusela
1b.	Wagqibela nini wena neqabane lakho elikuphando ukulalana?	<input type="text"/> <input type="text"/>	<input type="checkbox"/> iintsuku <input type="checkbox"/> iiveki <input type="checkbox"/> iinyanga
1c.	Kwizihlandlo samva nje, benisebenzise ikhondom?	<input type="checkbox"/> ewe <input type="checkbox"/> hayi	
2	Ngaphandle kweqabane lakho elikuphando, mangaphi amanye amaqabane okhe wabelana nawo ngesondo ukusukela kutyalelo lwakho lokugqibela lwesiqhelo?	<input type="text"/> <input type="text"/> <input type="text"/>	inani lamaqabane → If 0, go to item 3.
2a.	Kulamaqabane mangaphi amaqabane amatsha?	<input type="text"/> <input type="text"/> <input type="text"/>	inani lamaqabane amatsha
2b.	Ukususela kutyalelo lwakho lokugqibela lwesiqhelo, wabelana kangaphi ngesondo naye nabanina ngaphandle kweqabane (amaqabane) lakho lophando?	<input type="text"/> <input type="text"/> <input type="text"/>	inani lezihlundo zokwabelana ngesondo → If 0, go to item 3.
2b1.	Kulawo maxesha, sisetyenziswe kangaphi isingxobo sokuzikhusela?	<input type="text"/> <input type="text"/> <input type="text"/>	amaxesha ekusetyenziswe ngawo izingxobo zokuzikhusela

Item 3 is for females only. Males continue to item 4.

3	Ungaba usebenzisa ucwangciso ntsapho? Mark only the primary method.
<input type="checkbox"/> hayi okanye azikho <input type="checkbox"/> okomlomo <input type="checkbox"/> isithinteli nzala esifakwa ngaphakathi esibekekweni (luphu)	<input type="checkbox"/> ehlatywayo <input type="checkbox"/> ezifakelweyo <input type="checkbox"/> khondom
<input type="checkbox"/> Ukuvala ukungazali okanye ukukhutshwa kwesibekeko <input type="checkbox"/> ezinye: _____	

Item 4 is not interviewer-administered.

4	How many partners are enrolled for this index participant? <input type="text"/> number of partners → If only one partner, stop. If more than one enrolled partner, complete page 2 of the Index Follow-up Sexual Risk Behavior form (IFSX-2).
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Version 2.0, 15-01-05

Xhosa

Completed by: _____ (initials/date)

SAMPLE: DO NOT FAX TO DATAFAX

(Partners) 020

(IFSX-2) 210

Visit Code

Participant ID: <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> - <input type="text"/> <small style="display: block; text-align: center;">Site Couple I/P Chk</small>	Form Completion Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <small style="display: block; text-align: center;">dd mm yy</small>	
Index Follow-up Sexual Risk Behavior, page 2 <i>This is an interviewer-administered form. Read each item aloud to the participant.</i>		
<i>If only one partner participant enrolled with this index participant, do not complete this page of the form. Sexual behavior with additional partner participants is recorded here.</i>		
5	Partner #2 ID <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - 2 - <input type="text"/> <small style="display: block; text-align: center;">Site Couple I/P Chk</small>	
6	Ukusukela kutyalelo lwakho lokugqibela lwarhoqo, wabelane kangaphi ngesondo neqabane lakho elikuphando? <input type="text"/> <input type="text"/> <input type="text"/> <i>inani lezihlandlo zokwabelana ngesondo</i> <div style="text-align: right; margin-right: 50px;">→ <i>If 0, go to item 7.</i></div>	
6a.	Kulawo maxesha, sisetyenziswe kangaphi isingxobo sokuzikhusela? <input type="text"/> <input type="text"/> <input type="text"/> <i>amaxesha ekusetyenziswe ngawo izingxobo zokuzikhusela</i>	
6b.	Wagqibela nini wena neqabane lakho elikuphando ukulalana? <input type="text"/> <input type="text"/> <div style="margin-left: 20px;"> <input type="checkbox"/> iintsuku <input type="checkbox"/> iiveki <input type="checkbox"/> iinyanga </div>	
6c.	Kwisihlandlo samva nje, benisebenzise ikhondom? <input type="checkbox"/> ewe <input type="checkbox"/> hayi	
7	Partner #3 ID <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - 3 - <input type="text"/> <small style="display: block; text-align: center;">Site Couple I/P Chk</small>	
8	Ukusukela kutyalelo lwakho lokugqibela lwarhoqo, wabelane kangaphi ngesondo neqabane lakho elikuphando? <input type="text"/> <input type="text"/> <input type="text"/> <i>inani lezihlandlo zokwabelana ngesondo</i> <div style="text-align: right; margin-right: 50px;">→ <i>If 0, end of form.</i></div>	
8a.	Kulawo maxesha, sisetyenziswe kangaphi isingxobo sokuzikhusela? <input type="text"/> <input type="text"/> <input type="text"/> <i>amaxesha ekusetyenziswe ngawo izingxobo zokuzikhusela</i>	
8b.	Wagqibela nini wena neqabane lakho elikuphando ukulalana? <input type="text"/> <input type="text"/> <div style="margin-left: 20px;"> <input type="checkbox"/> iintsuku <input type="checkbox"/> iiveki <input type="checkbox"/> iinyanga </div>	
8c.	Kwisihlandlo samva nje, benisebenzise ikhondom? <input type="checkbox"/> ewe <input type="checkbox"/> hayi	
Version 1.0, 27-10-04	Xhosa	Completed by: _____ (initials/date)

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020

(PESX) 120

Visit Code 00.0

Participant ID: - - <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Form Completion Date: <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>
Partner Enrollment Sexual Risk Behavior <i>This is an interviewer-administered form. Read each item aloud to the participant.</i>	
<p>Now I'm going to ask you about your sexual practices. While some of this information may be embarrassing or difficult to remember, please try to give your best answers and be as honest as you can. Whenever "sex" or "sexual intercourse" is stated, it includes vaginal and anal sex, but not oral sex. The term "condom" refers to either a male or female condom.</p>	
1	<p>In the past month, how many times did you have sexual intercourse with your study partner? <i>number of sex acts</i></p> <p style="text-align: right;">→ If 0, go to item 2.</p> <p>1a. Of those times, how often was a condom used? <i>number of times condom used</i></p>
2	<p>When having sex, do you and your study partner ever use anything to reduce the secretions or make the vagina dry?</p> <p><input type="checkbox"/> yes <input type="checkbox"/> no → If no, go to item 3.</p> <p>2a. What have you used to make the vagina dry? _____</p> <p>2b. How often do you use something to make the vagina dry?</p> <p><input type="checkbox"/> rarely <input type="checkbox"/> sometimes <input type="checkbox"/> most of the time <input type="checkbox"/> always</p>
<i>Item 3 is for females only. Males continue to item 4.</i>	
3	<p>Are you currently using birth control? <i>Mark only the primary method.</i></p> <div style="display: flex; flex-wrap: wrap;"> <div style="width: 33%;"><input type="checkbox"/> no/none</div> <div style="width: 33%;"><input type="checkbox"/> injectable</div> <div style="width: 33%;"><input type="checkbox"/> tubal ligation/hysterectomy</div> <div style="width: 33%;"><input type="checkbox"/> oral</div> <div style="width: 33%;"><input type="checkbox"/> implants</div> <div style="width: 33%;"><input type="checkbox"/> other, specify: _____</div> <div style="width: 33%;"><input type="checkbox"/> IUD</div> <div style="width: 33%;"><input type="checkbox"/> condoms only</div> </div>
<i>Item 4 is not interviewer-administered.</i>	
4	<p>In the past three months, has the participant taken HIV medication because of an exposure to HIV? <input type="checkbox"/> yes <input type="checkbox"/> no → If no, end of form.</p> <p>4a. For how many days was medication taken? <i>number of days</i></p>
Version 1.0, 27-10-04	English
Completed by: _____ (initials/date)	

SAMPLE: DO NOT FAX TO DATAFAX



Visit Code 00.0

(Partners) 020

(PESX) 120

Participant ID: - - <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Form Completion Date: / / <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>
Partner Enrollment Sexual Risk Behavior <i>This is an interviewer-administered form. Read each item aloud to the participant.</i>	
Ngoku ndizakukubiza ngezesondo. Nangona olu lwazi lusenokubanga iintloni okanye kubenzima ukukhumbula, nceda uzame kangangoko unakho ukunika impendulo enyanisekileyo. Nanini na kuthethwa ngesondo okanye ukwabelana ngesondo, kubandakanya ukwabelana ngesondo ebufazini nangasemva kodwa hayi emlonjeni. Igama elithi khondom libhekiselele kwikhondom yabafazi okanye eyamadoda.	
1	Kule nyanga iphelileyo, wabelane kangaphi ngesondo neqabane lakho elikuphando? <input style="width: 40px; height: 20px; border: 1px solid black;" type="text"/> inani lezihlambululo zokwabelana ngesondo If 0, go to item 2.
1a.	Kulawo maxesha, sisetyenziswe kangaphi isingxobo sokuzikhusela? <input style="width: 40px; height: 20px; border: 1px solid black;" type="text"/> amaxesha ekusetyenziswe ngawo izingxobo zokuzikhusela
2	Xa nisabelana ngesondo, wena neqabane lakho lophando nakhe nasebenzisa nto na ngamanye amaxesha ukunciphisa incindi okanye ukomisa ubufazi? <input type="checkbox"/> ewe <input type="checkbox"/> hayi If no, go to item 3.
2a.	Benikhe nasebenzisa ntoni ukomisa ubufazi? _____
2b.	Kuxhaphake kangakanani ukusebenzisa into yokomisa ubufazi bakho? <div style="display: flex; justify-content: space-around; font-size: small;"> <input type="checkbox"/> kunqabile <input type="checkbox"/> ngamanye amaxesha <input type="checkbox"/> amaxesha amaninzi <input type="checkbox"/> ngalo lonke ixesha </div>
Item 3 is for females only. Males continue to item 4.	
3	Ungaba usebenzisa ucwangciso ntsapho? <i>Mark only the primary method.</i> <div style="display: flex; flex-wrap: wrap; font-size: small;"> <div style="width: 33%;"><input type="checkbox"/> hayi okanye azikho</div> <div style="width: 33%;"><input type="checkbox"/> ehlatywayo</div> <div style="width: 33%;"><input type="checkbox"/> Ukuvala ukungazali okanye ukukhutshwa kwesibeleko</div> <div style="width: 33%;"><input type="checkbox"/> okomlomo</div> <div style="width: 33%;"><input type="checkbox"/> ezifakelweyo</div> <div style="width: 33%;"><input type="checkbox"/> ezinye: _____</div> <div style="width: 33%;"><input type="checkbox"/> isithinteli nzala esifakwa ngaphakathi esibelekweni (luphu)</div> <div style="width: 33%;"><input type="checkbox"/> khondom</div> </div>
Item 4 is not interviewer-administered.	
4	In the past three months, has the participant taken HIV medication because of an exposure to HIV? <input type="checkbox"/> yes <input type="checkbox"/> no If no, end of form.
4a.	For how many days was medication taken? <input style="width: 40px; height: 20px; border: 1px solid black;" type="text"/> number of days
<div style="border: 1px solid black; height: 40px; margin-top: 10px;"></div>	
Version 1.0, 27-10-04	Xhosa Completed by: _____ (initials/date)

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020

(PFSX) 220

Visit Code

Participant ID: <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Visit Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>	
Partner Follow-up Sexual Risk Behavior <i>This is an interviewer-administered form. Read each item aloud to the participant.</i>		
Now I'm going to ask you about your sexual practices. While some of this information may be embarrassing or difficult to remember, please try to give your best answers and be as honest as you can. Whenever "sex" or "sexual intercourse" is stated, it includes vaginal and anal sex, but not oral sex. The term "condom" refers to either a male or female condom.		
1 In the past month, how many times did you have sexual intercourse with your study partner? 1a. Of those times, how often was a condom used?	<input type="text"/> <input type="text"/> <input type="text"/> number of sex acts → If 0, go to item 2. <input type="text"/> <input type="text"/> <input type="text"/> number of times condom used	
1b. How long has it been since you last had sex with your study partner?	<input type="text"/> <input type="text"/> <input type="checkbox"/> days <input type="checkbox"/> weeks <input type="checkbox"/> months	
1c. During this most recent encounter, was a condom used?	<input type="checkbox"/> yes <input type="checkbox"/> no	
2 Besides the study partner, how many partners have you had sex with in the past month? 2a. How many of these are new partners? 2b. In the past month, how many times did you have sexual intercourse with someone other than your study partner? 2b1. Of those times, how often was a condom used?	<input type="text"/> <input type="text"/> <input type="text"/> number of partners → If 0, go to item 3. <input type="text"/> <input type="text"/> <input type="text"/> number of new partners <input type="text"/> <input type="text"/> <input type="text"/> number of sex acts → If 0, go to item 3. <input type="text"/> <input type="text"/> <input type="text"/> number of times condom used	
Item 3 is for females only. Males continue to item 4.		
3 Are you currently using birth control? <i>Mark only the primary method.</i>	<div style="display: flex; flex-wrap: wrap;"> <div style="width: 33%;"><input type="checkbox"/> no/none</div> <div style="width: 33%;"><input type="checkbox"/> injectable</div> <div style="width: 33%;"><input type="checkbox"/> tubal ligation/hysterectomy</div> <div style="width: 33%;"><input type="checkbox"/> oral</div> <div style="width: 33%;"><input type="checkbox"/> implants</div> <div style="width: 33%;"><input type="checkbox"/> other, specify: _____</div> <div style="width: 33%;"><input type="checkbox"/> IUD</div> <div style="width: 33%;"><input type="checkbox"/> condoms only</div> </div>	
Item 4 is not interviewer-administered.		
4 Since the last quarterly visit, has the participant taken HIV medication because of an exposure to HIV? 4a. For how many days was medication taken?	<input type="checkbox"/> yes <input type="checkbox"/> no → End of form. <input type="text"/> <input type="text"/> number of days	
Version 1.0, 27-10-04	English	Completed by: _____ (initials/date)

SAMPLE: DO NOT FAX TO DATAFAX

(Partners) 020

(PFSX) 220

Visit Code

Participant ID: <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Visit Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>
Partner Follow-up Sexual Risk Behavior <i>This is an interviewer-administered form. Read each item aloud to the participant.</i>	
Ngoku ndizakukubuza ngezesondo. Nangona olu lwazi lusenkubanga iintloni okanye kubenzima ukukhumbula, nceda uzame kangangoko unakho ukunika impendulo enyanisekileyo. Nanini na kuthethwa ngesondo okanye ukwabelana ngesondo, kubandakanya ukwabelana ngesondo ebufazini nangasemva kodwa hayi emlonyeni. Igama elithi khondom libhekiselele kwikhondom yabafazi okanye eyamadoda.	
1 Kule nyanga iphelileyo, wabelane kangaphi ngesondo neqabane lakho elikuphando?	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> inani lezihlundo zokwabelana ngesondo If 0, go to item 2.
1a. Kulawo maxesha, sisetyenziswe kangaphi isingxobo sokuzikhusela?	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> amaxesha ekusetyenziswe ngawo izingxobo zokuzikhusela
1b. Wagqibela nini wena neqabane lakho elikuphando ukutalana?	<input type="checkbox"/> iintsuku <input type="checkbox"/> iiveki <input type="checkbox"/> iinyanga
1c. Kwisihlandlo samva nje, benisebenzise ikhondom?	<input type="checkbox"/> ewe <input type="checkbox"/> hayi
2 Ngaphandle kweqabane lakho elikuphando, mangaphi amanye amaqabane okhe wabelana nawo ngesondo kulenyanga iphelileyo?	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> inani lamaqabane If 0, go to item 3.
2a. Kulamaqabane mangaphi amaqabane amatsha?	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> inani lamaqabane amatsha
2b. Kulenyanga iphelileyo, wabelane kangaphi ngesondo nomnye umntu ngaphandle kweqabane lakho elikuphando?	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> inani lezihlundo zokwabelana ngesondo If 0, go to item 3.
2b1. Kulawo maxesha, sisetyenziswe kangaphi isingxobo sokuzikhusela?	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> amaxesha ekusetyenziswe ngawo izingxobo zokuzikhusela
Item 3 is for females only. Males continue to item 4.	
3 Ungaba usebenzisa ucwangciso ntsapho? <i>Mark only the primary method.</i>	<div style="display: flex; flex-wrap: wrap;"> <div style="width: 33%;"><input type="checkbox"/> hayi okanye azikho</div> <div style="width: 33%;"><input type="checkbox"/> ehlatywayo</div> <div style="width: 33%;"><input type="checkbox"/> Ukuvala ukungazali okanye ukukhutshwa kwesibeleko</div> <div style="width: 33%;"><input type="checkbox"/> okomlomo</div> <div style="width: 33%;"><input type="checkbox"/> ezifakelweyo</div> <div style="width: 33%;"><input type="checkbox"/> ezinye: _____</div> <div style="width: 33%;"><input type="checkbox"/> isithinteli nzala esifakwa ngaphakathi esibelekweni (luphu)</div> <div style="width: 33%;"><input type="checkbox"/> khondom</div> </div>
Item 4 is not interviewer-administered.	
4 Since the last quarterly visit, has the participant taken HIV medication because of an exposure to HIV?	<input type="checkbox"/> yes <input type="checkbox"/> no If no, End of form.
4a. For how many days was medication taken?	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> number of days
Version 1.0, 27-10-04 Xhosa Completed by: _____ (initials/date)	

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020

(EDT-1) 170

Visit Code 00.0

Participant ID: - - <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Form Completion Date: <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>	
Enrollment Diagnoses and Treatment, page 1		
1 Syndromic Diagnoses (not needing laboratory confirmation)		
1a. Urethritis or urethral discharge: <input type="checkbox"/> not done <input type="checkbox"/> yes <input type="checkbox"/> no		
1b. Genital ulcer disease (GUD): <input type="checkbox"/> not done <input type="checkbox"/> yes <input type="checkbox"/> no		
1c. Genital herpes (HSV): <input type="checkbox"/> not done <input type="checkbox"/> yes <input type="checkbox"/> no		
1d. Lymphogranuloma venereum: <input type="checkbox"/> not done <input type="checkbox"/> yes <input type="checkbox"/> no		
<i>Items 1e-1g are for women only. Males continue to item 2.</i>		
1e. Vaginitis or vaginal discharge: <input type="checkbox"/> not done <input type="checkbox"/> yes <input type="checkbox"/> no		
1f. Cervicitis or cervical discharge: <input type="checkbox"/> not done <input type="checkbox"/> yes <input type="checkbox"/> no		
1g. Pelvic inflammatory disease (PID): <input type="checkbox"/> not done <input type="checkbox"/> yes <input type="checkbox"/> no		
2 Syphilis test (Required at Enrollment.)		
2a. Result: <input type="checkbox"/> not done <input type="checkbox"/> done → Result: <input type="checkbox"/> negative → Go to item 3. <div style="margin-left: 400px;"><input type="checkbox"/> weakly reactive → Go to item 2b.</div> <div style="margin-left: 400px;"><input type="checkbox"/> positive → Go to item 2a1. </div>		
2a1. If positive, titer: 1: 		
2b. Syphilis confirmatory test: <input type="checkbox"/> not done <input type="checkbox"/> done → Result: <input type="checkbox"/> negative <input type="checkbox"/> positive		
2c. Treatment for syphilis given? <input type="checkbox"/> yes <input type="checkbox"/> no		
Continue to Item 3 on page 2.		
Version 1.0, 27-10-04	English	Completed by: _____ (initials/date)

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020

(EDT-2) 175

Visit Code 00.0

Participant ID: - - - <div style="display: flex; justify-content: space-around; font-size: small;"> Site Couple I/P Chk </div>	Form Completion Date: / / <div style="display: flex; justify-content: space-around; font-size: small;"> dd mm yy </div>
Enrollment Diagnoses and Treatment, page 2	
3 Were any additional laboratory tests done for etiologic diagnosis of STDs? <input type="checkbox"/> yes <input type="checkbox"/> no → If no, go to item 4.	
3a. Gonorrhoeae: <input type="checkbox"/> not done <input type="checkbox"/> done → Result: <input type="checkbox"/> negative <input type="checkbox"/> positive	
3b. Chlamydia: <input type="checkbox"/> not done <input type="checkbox"/> done → Result: <input type="checkbox"/> negative <input type="checkbox"/> positive	
3c. Chancroid: <input type="checkbox"/> not done <input type="checkbox"/> done → Result: <input type="checkbox"/> negative <input type="checkbox"/> positive	
3d. Trichomonas: <input type="checkbox"/> not done <input type="checkbox"/> done → Result: <input type="checkbox"/> negative <input type="checkbox"/> positive	
<i>Items 3e-3f are for women only. Males continue to item 4.</i>	
3e. Bacterial Vaginosis: <input type="checkbox"/> not done <input type="checkbox"/> done → Result: <input type="checkbox"/> negative <input type="checkbox"/> positive	
3f. Candidiasis: <input type="checkbox"/> not done <input type="checkbox"/> done → Result: <input type="checkbox"/> negative <input type="checkbox"/> positive	
4 Was antibiotic treatment given? <input type="checkbox"/> yes <input type="checkbox"/> no → If no, go to item 5.	
4a. Name(s) of antibiotic(s) given: <i>(Use generic names.)</i> _____	
5 Was acyclovir treatment given? <input type="checkbox"/> yes <input type="checkbox"/> no	
<i>Items 6 is for women only.</i>	
6 Pap smear result: Use Bethesda system. Perform this test where pap smear is the standard of care.	
<input type="checkbox"/> not done or not assessable <input type="checkbox"/> normal <input type="checkbox"/> ASC <input type="checkbox"/> LSIL (CIN 1) <input type="checkbox"/> HSIL (CIN 2, CIN 3) <input type="checkbox"/> SCC <input type="checkbox"/> other: _____	
Version 1.0, 27-10-04	English Completed by: _____ (initials/date)

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020

(FDT-1) 270
Visit Code Participant ID: - - -
Site Couple I/P ChkForm Completion Date:
dd mm yy

Follow-up Diagnoses and Treatment, page 1

- 1 Pregnancy test result: **Women only. Males continue to item 2.**
Perform pregnancy test at all quarterly visits (except exit) for female index participants, and as clinically indicated for all female participants (index and partner).

☐ negative ☐ positive ☐ not done

→ If positive, complete Pregnancy Report form.

- 2 **Syndromic Diagnoses** (not needing laboratory confirmation)

2a. Urethritis or urethral discharge: ☐ not done ☐ yes ☐ no

2b. Genital ulcer disease (GUD): ☐ not done ☐ yes ☐ no

2c. Genital herpes (HSV): ☐ not done ☐ yes ☐ no

2d. Lymphogranuloma venereum: ☐ not done ☐ yes ☐ no

Items 2e–2g are for women only. Males continue to item 3.

2e. Vaginitis or vaginal discharge: ☐ not done ☐ yes ☐ no

2f. Cervicitis or cervical discharge: ☐ not done ☐ yes ☐ no

2g. Pelvic inflammatory disease (PID): ☐ not done ☐ yes ☐ no

- 3 **Syphilis test** (Required at study exit.) ☐ yes ☐ no → If no, go to item 4.

3a. Result: ☐ not done ☐ done → Result: ☐ negative → Go to item 4.
☐ weakly reactive → Go to item 3b.
☐ positive → Go to item 3a1.

3a1. If positive, titer: 1:

3b. Syphilis confirmatory test: ☐ not done ☐ done → Result: ☐ negative ☐ positive

3c. Treatment for syphilis given? ☐ yes ☐ no

Continue to item 4 on page 2.

Version 1.0, 27-10-04

English

Completed by: _____ (initials/date)

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020

(FDT-2) 275

Visit Code

Participant ID: - - -
Site Couple I/P Chk

Form Completion Date:
dd mm yy

Follow-up Diagnoses and Treatment, page 2

- 4 Were any additional laboratory tests done for etiologic diagnosis of STDs? ☐ yes ☐ no → If no, go to item 5.
- 4a. Gonorrhoeae: ☐ not done ☐ done → Result: ☐ negative ☐ positive
- 4b. Chlamydia: ☐ not done ☐ done → Result: ☐ negative ☐ positive
- 4c. Chancroid: ☐ not done ☐ done → Result: ☐ negative ☐ positive
- 4d. Trichomonas: ☐ not done ☐ done → Result: ☐ negative ☐ positive

Items 4e-4f are for women only. Males continue to item 5.

- 4e. Bacterial Vaginosis: ☐ not done ☐ done → Result: ☐ negative ☐ positive
- 4f. Candidiasis: ☐ not done ☐ done → Result: ☐ negative ☐ positive

- 5 Was antibiotic treatment given? ☐ yes ☐ no → If no, go to item 6.

5a. Name(s) of antibiotic(s) given:
(Use generic names.) _____

- 6 Was acyclovir treatment given? ☐ yes ☐ no

Items 7 is for women only.

- 7 Pap smear result: Use Bethesda system. Perform this test where pap smear is the standard of care.

- ☐ not done or not assessable
- ☐ normal
- ☐ ASC
- ☐ LSIL (CIN 1)
- ☐ HSIL (CIN 2, CIN 3)
- ☐ SCC
- ☐ other: _____

SAMPLE: DO NOT FAX TO DATAFAX
(Partners) 020■■■■■■■■■■
(PREG) 330Visit Code

Participant ID: <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> - <input type="text"/> Site Couple I/P Chk		Form Completion Date: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> dd mm yy	
Pregnancy Report <i>If the index participant has not already stopped drug due to an SAE, complete the Study Drug Interruption Log.</i>			
1	Date of first day of last menstrual period, if known: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> dd mm yy		
2	Date of last negative pregnancy result obtained by site: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> dd mm yy		
3	Estimated date of delivery: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> dd mm yy		
4	How was this date determined? <input type="checkbox"/> ultrasound <input type="checkbox"/> fundal height <input type="checkbox"/> LMP <input type="checkbox"/> don't know <input type="checkbox"/> other: _____		
5	Comments: _____ _____ _____ _____		
Version 1.0, 27-10-04		English	Completed by: _____ (initials/date)

Appendix E: Ethics and Faculty approval letters

D1 – Study Proposal

	<h1>University of Cape Town</h1> <h2>Faculty of Health Sciences</h2> <h3>Form D1: Study proposal - approval</h3>
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SUBMISSION OF STUDY PROPOSAL FOR A MASTER'S OR DOCTORAL DEGREE AFTER ETHICAL APPROVAL

PLEASE NOTE: This form must not be sent to Ethics

I would like to submit the following proposal and supporting documentation for consideration by the Dissertations Committee (after Ethics approval).

Signature (Candidate): Namale P.E

NAME OF CANDIDATE	NAMALE PHIONA ENID
STUDENT NUMBER	NMLPHI 002
QUALIFICATIONS	MEDICAL DOCTOR
TITLE OF PROPOSED PROJECT (Proposal attached)	SEXUAL BEHAVIOUR OF HETERO-SEXUAL HIV DISCORDANT COUPLES BEFORE AND AFTER COUNSELLING & EDUCATION AS PART OF AN HIV PREVENTION TRIAL
DEPARTMENT	PUBLIC HEALTH
LEVEL OF PROJECT - Master's or Doctoral	MASTER'S
PROPOSAL NOTED BY DIVISIONAL POST-GRADUATE REPRESENTATIVE	Postgraduate representative. Signature:
PROPOSAL SUPPORTED BY DEPARTMENTAL RESEARCH COMMITTEE	Chair, Department Research Committee: Signature: <i>[Signature]</i>
PROPOSAL APPROVED BY (Delete any one if not applicable) Human Ethics Committee, ERC No: 213/2004 Animal Ethics Committee, ERC No:	(Attach Ethics approval letter)
FINAL SUBMISSION APPROVED BY SUPERVISOR	Supervisor: <i>[Signature]</i> D.T. GREEFF
FINAL SUBMISSION APPROVED BY HEAD OF DIVISION	Head of Division: <i>[Signature]</i>

If ethics approval not required please explain in COMMENTS

COMMENTS:

This study is using secondary data. This data has no participant identifiers. This primary study got UCT ethical approval REC REF 213/2004.

Prof Leslie London-Director
UCT - School of Public Health & Family Medicine
Faculty of Health Sciences
Anzio Road, Observatory, 7925
Tel: 021 406 6524 Fax: 021 406 6163

UNIVERSITY OF CAPE TOWN



Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • Facsimile [021] 406 6411
e-mail: lamees.emjedi@uct.ac.za

11 April 2007

REC REF: 213/2004

Dr D Coetzee
Infectious Disease Epidemiology Unit
Public Health & Family Medicine

Dear Dr Coetzee

**PROJECT TITLE: PHASE III RANDOMISED PLACEBO-CONTROLLED TRIAL OF HSV-2
SUPPRESSION TO PREVENT HIV TRANSMISSION AMONG HIV DISCORDANT COUPLES**

Thank you for your letter to the Research Ethics Committee dated 03 April 2007.

It is a pleasure to inform you that the Ethics Committee has granted ongoing approval for the above-mentioned trial for one year. This approval is granted for Protocol Version 4.1.1 dated 15 December 2005.

Thank you for submitting the report in accordance with US regulations.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

Pp A/PROF. M. BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

lemjedi

Appendix F: Manuscript instructions to authors

Instructions for Authors

AIDS and Behavior

Manuscript Submission

Seth C. Kalichman, Ph.D.

Center for HIV Prevention & Intervention

2006 Hillside Road, Unit 1248

University of Connecticut

Storrs, CT 06269

Email: aidsandbehavior@yahoo.com

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AIDS and Behavior now offers the opportunity to publish abstracts for articles in English and Spanish. Although not required, I am hoping that you will take advantage of this chance to broaden access of your work. If you would like to include your Abstract in Spanish, please be sure that your Abstract is in the proper format and finalized. Be sure to remove all subheadings from the Abstract so that it reads as a continuous narrative of no more than 150 words in English. Then translate your final Abstract into Spanish. Upload the English version in the Editorial Manager System step for Abstracts and include both the English and Spanish versions in your Manuscript file that you upload into the system. The two abstracts should be placed together, first the English followed by the Spanish on a separate pages. Label the Spanish version "Resumen".

Manuscripts should be submitted to the Editor through Springer's Editorial Manager Peer review system at: <http://aibe.edmgr.com>

Manuscript Preparation

- Type double-spaced on one side of 8 ½ × 11-inch white paper using generous margins on all sides, (including copies of all illustrations and tables).
- A title page is to be provided and should include the title of the article, authors name (no degrees), authors affiliation, and suggested running head. The affiliation should comprise the department, institution (usually university or company), city, and state (or nation) and should be typed as a footnote to the author's name. The suggested running head should be less than 80 characters (including spaces) and should comprise the article title or an abbreviated version thereof. For office purposes, the title page should include the complete mailing address, telephone number, fax number, and email address of the one author designated to review proofs.
- With the exception of Brief Reports and Behavioral Surveillance Reports, initial submissions to AIDS and Behavior do not have word or page limits. Briefer and more succinct papers tend to review better and papers may be reduced in length as part of the review process. However, the length of the original submission is left to author discretion.
- An abstract is to be provided, preferably no longer than 150 words.
- A list of 4-5 key words is to be provided directly below the abstract. Key words should express the precise content of the manuscript, as they are used for indexing purposes.
- All sections should carry headings (such as INTRODUCTION, METHODS, RESULTS, DISCUSSION, CONCLUSIONS, etc.), typed flush left. All acknowledgments (including those for grant and financial support) should be typed in one paragraph (so-headed) on a separate page that directly precedes the References section.
- Illustrations (photographs, drawings, diagrams, and charts) are to be numbered in one consecutive series of Arabic numerals. The captions for illustrations should be typed on a separate sheet of paper. All illustrations must be complete and final, i.e., camera-ready. Photographs should be large, glossy prints, showing high

contrast. Drawings should be high quality laser prints or should be prepared with india ink. Either the original drawings or good-quality photographic prints are acceptable. Artwork for each figure should be provided on a separate sheet of paper. Identify figures on the back with authors name and number of the illustration. Electronic artwork submitted on disk should be in the TIFF or EPS format (1200 dpi for line and 300 dpi for halftones and grayscale art). Color art should be in the CYMK color space. Artwork should be on a separate disk from the text, and hard copy must accompany the disk.

- Tables should be numbered (with Roman numerals) and referred to by number in the text. Each table should be typed on a separate sheet of paper. Center the title above the table, and type explanatory footnotes (indicated by superscript lowercase letters) below the table.
- AIDS and Behavior does not have a limit on number of authors. However, if deemed to be excessive the editor may request author justifications and reductions.

AIDS and Behavior uses Vancouver style as outlined in the American Medical Association Manual of style: A Guide for Authors and Editors, 10th Edition.

A reference number is allocated to a source in the order in which it is cited in the text. In text, identify references as Arabic numerals in brackets (1). If the source is referred to again, the same number is used. References are listed in numerical order in the Reference List at the end of the paper. Do not alphabetize. Use abbreviated names of journals according to the journal list in PubMed. List all authors and/or editors up to 6; if more than 6, list the first 3 followed by "et al." The following are examples.

1) McKirnan DJ, Vanable PA, Ostrow DG, Hope B. Expectancies of sexual "escape" and sexual risk among drug and alcohol-involved gay and bisexual men. *J Subst Abuse*. 2001;13(1-2):137-54.

2) van der Straten A, Cheng H, Moore, J et al. The use of the diaphragm instead of condoms in a phase III diaphragm trial. *AIDS Behav*. 2009; 13(3):564-72.

3) Eaton LA, Kalichman SC. Changes in transmission risk behaviors across stages of HIV disease among people living with HIV. *J Assoc Nurses AIDS Care*. 2009 Jan-Feb;20(1):39-49.

4) Bangsberg D, Hecht F, Charlebois E, Chesney M, Moss A. Comparing objectives measures of adherence to HIV antiretroviral therapy: electronic medication monitors and unannounced pill counts. *AIDS Behav* 2001, 5:275–281.

5) Richman D, Bozzette S, Morton S, et al. The prevalence of antiretroviral drug resistance in the US. Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, 2001 [abstract LB-17].

6) Hirsch MS, D'Aquila RT, Kaplan JC. Antiretroviral therapy. In: DeVita VT, Hellman S, Rosenberg SA, eds. *AIDS: Biology, Diagnosis, Treatment and Prevention*. 4th ed. Philadelphia, PA: Lippincott-Raven; 1997.

7) Ray SC. Simplot for Windows, version 2.5. Available at: <http://www.med.jhu.edu/deptmed/sray/download/>. Accessed November 7, 2001.

Verify that every instance of a number in text corresponds to the numbered reference.

Footnotes should be avoided. When their use is absolutely necessary, footnotes should be numbered consecutively using Arabic numerals and should be typed at the bottom of the page to which they refer. Place a line above the footnote, so that it is set off from the text. Use the appropriate superscript numeral for citation in the text.

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University of Cape Town